Relationship Between Vitamin D Deficiency and Markers of Metabolic Syndrome Among Overweight and Obese Adults

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Abstract- In recent years, metabolic syndrome, obesity, diabetes and cardiovascular disease has had a tremendous elevation growth. Many studies have demonstrated negative correlation between vitamin D deficiency and indexes of metabolic syndrome in obese patients. This study was designed to find the relation between vitamin D deficiency and markers of metabolic syndrome among overweight and obese adults referred to obesity center of Shahid Sadoughi hospital in 2014. Eighty-nine overweight and obese adults (79 women and 10 men), who 13 subjects were overweight and 76 subjects were obese were recruited in this cross-sectional study. Total cholesterol, high-density lipoprotein cholesterol, triglyceride, plasma glucose and vitamin D were measured. IDF criteria were used for identifying subjects with metabolic syndrome. Demographic questionnaire was completed. Statistical analysis was performed using SPSS version 16.0. Fisher exact test, logistic regression, and Spearman correlation coefficient were used. The frequency of vitamin D deficiency was 93.2%. According to IDF criteria, the frequency of metabolic syndrome was 36%. There was no significant relationship between vitamin D deficiency and metabolic syndrome. Among metabolic syndrome indicators, there was a significant direct relationship between vitamin D level with FBS (P=0.013) and SBP (P=0.023). There was no significant relationship between vitamin D deficiency and metabolic syndrome. Due to the lack of relationship between vitamin D deficiency and metabolic syndrome, small number of participants in this study and very low case of normal vitamin D level, further studies are needed.

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Introduction

Vitamin D deficiency is a major public health problem in the world. The prevalence of vitamin D deficiency is higher in Asian countries. Several studies indicate a high prevalence of vitamin D deficiency in Iran (1,2). Vitamin D can be synthesized through sunlight exposure in the skin. It can also be obtained from a balanced diet, although foods sources of vitamin D are not enough to meet the body's requirements. Darkening of the skin, obesity and decreased physical activity can reduce the intake and absorption of vitamin D (1). Vitamin D has other vital functions in addition to the regulation of calcium homeostasis and bone health (1).

Recent clinical and epidemiologic studies have been proposed vitamin D deficiency as a risk factor for the development and progression of hyperlipidemia, hypertension, obesity, insulin resistance, type 2 diabetes, cardiovascular diseases (1-3). Mackay and coworker demonstrated the association of vitamin D and vitamin D receptor gene polymorphisms with chronic inflammation, insulin resistance and metabolic syndrome components in type 2 diabetic Egyptian patients (4). However, some studies stated that the amount of vitamin D as an independent variable has no effect (5).

On the other hand, metabolic syndrome, a combination of factors such as glucose intolerance, central obesity, hypertension, and dyslipidemia is an important risk factor for type II diabetes and cardiovascular diseases. Metabolic syndrome is one of

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the major health problems in the world (6,7). The cause of metabolic syndrome is unclear but genetic, and environment may be essential factors for initiation and progression of it. Diet is one of the important factors in the development of this problem (8). Studies on the role of diet in this field are limited. Most studies are about macronutrients, and less has been investigated the role of micronutrients in this field.

Given the controversial studies and increased the prevalence of vitamin D deficiency and metabolic syndrome, the need to do further studies in this field is felt. The aim of this study was to investigate the relationship between vitamin D deficiency with markers of metabolic syndrome in overweight and obese adults came to obesity clinic in Yazd province.

Materials and Methods

This is a cross-sectional study conducted on eighty-nine overweight and obese adults (BMI>25 kg/m2) aged 18-60-year-old in the obesity research center of Shahid Sadoughi University of Medical Sciences (Baghaeipour Clinic), Yazd, Iran in 2015. Exclusion criteria were hepatic or renal disease, mal-absorptive disorders, and use of contraceptive pills or drugs that may affect lipid profile and/or metabolic parameters, pregnancy, and lactation, currently on weight loss medications, participating in commercial weight loss programs.

Body height in centimeters (cm) and weight in kilograms (kg) was measured by minimal clothing without shoes using Seca scale (Seca, Hamburg, Germany). Body Mass Index (BMI) was calculated as weight (kg) /squared height (meters). Waist circumference (WC) was measured using a non-elastic type without imposing a burden on the body with the accuracy of one centimeter. The waist was defined as the middle of the interval between the lower rib and the iliac crest. Blood pressure (BP) was measured in seated position after a rest of at least 15 minutes, of the right arm, twice from a distance of at least 30 seconds using a standard mercury sphygmomanometer (ALPK2, Japan). All measurements were performed by one person, a dietitian using the same devices throughout the study.

Metabolic syndrome was defined according to the definition of International Diabetes Federation (IDF) criteria which is the presence of Central obesity (WC ≥ 94 cm in men or ≥80 cm women), plus at least two of the following items: Serum triglyceride (TG) levels ≥ 150 mg/dl, or those who are undergoing drug therapy; high density lipoprotein (HDL) cholesterol < 40 mg/dl in men or <50 mg/dl in women; systolic blood pressure (SBP) ≥ 130 mm Hg; diastolic systolic blood pressure (DBP) ≥85 mmHg or patients treated for hypertension; fasting blood sugar (FBS) ≥ 100 mg/dl or previously diagnosed type 2 diabetes (9).

All participants signed a consent form before participating in this study, and their demographic information was collected by a questionnaire. Also study protocol was approved by the ethics committee of ShahidSadoughi University of Medical Science, Yazd, Iran.

Venous blood sample was obtained after 12 hours fasting. FBS, HDL and TG levels were measured by enzymatic methods (PARS AZMOON-IRAN). Serum 25-hydroxy vitamin D was assessed using the DiaSorin RIA (Stillwater, MN, USA)/ the LAISON(R) 25 OH Vitamin D Total Assay. The assay sensitivity was 1.5 ng/ml, and intra assay coefficient of variation (CV) was below 12%. The concentrationof less than 30 ng/ml considered as deficiency and 30ng/ml and above considered as normal.

Statistical analysis

Statistical analyses were performed using the SPSS (version 16.0; SPSS, Chicago, IL). Fisher exact test was used to determine the association between metabolic syndrome components and vitamin D deficiency. Regression analysis was performed to investigate the relationships of each of metabolic syndrome risk factor with vitamin 25(OH) D level. Spearman coefficient of correlation was used to assess thelinear correlation between 25(OH) D and other variables. Data were considered statistically significant if *P* were less than 0.05.

Results

A total of 89 overweight or obese adults (79 female and 10 male, 33.07±10.87-year-old) were included in this study. Baseline characteristics of participants were shown in Table 1.

Eighty-three of them (93.2%) had vitamin D deficiency (<30 ng/ml), and 27 persons (36%) had metabolic syndrome. There was no significant relationship between the frequency of vitamin D deficiency and metabolic syndrome (*P*=0.15).

The relationship between 25 (OH) D statuses and the frequency of metabolic syndrome components was assessed with Fisher exact test (Tables 2). The frequency of SBP <130 mmHg in the group with vitamin D deficiency was significantly higher than the group with normal vitamin D levels (*P*=0.023). Moreover, the

frequency of FBS<100 mg/dl in subjects with vitamin D deficiency was significantly higher than subjects with normal vitamin D levels (*P*=0.013). No significant relationship was found between the frequency of other components of the metabolic syndrome and vitamin D status (*P*>0.05).

According to table 3, based on correlation coefficient, there were significant inverse correlation between vitamin D deficiency with FBS (*P*=0.007) and also SBP (*P*=0.03) (correlation coefficient=0.29 and 0.22 respectively). But there was no correlation with other parameters (*P*>0.05). The logistic regression model in this study was not significant (*P*=0.89, Table 4).

Table 1. Baseline characteristics of study participants

Variables	Mean±SD
Age (y)	33.07±10.87
BMI (kg/m^2)	35.2±5.5
Waist circumference (cm)	103.71±16.25
HDL-C (mg/dl)	58.16±16.05
LDL-C (mg/dl)	91.16±26.6
TG (mg/dl)	160.03±104.12
Total cholesterol (mg/dl)	182.2±32.41
Vitamin D (ng/ml)	13.8±11.36

Table 2. The relationship between metabolic syndrome components frequency and vitamin D status

Variables	Classification	Vitamin D levels		*P*
		<30 ng/ml	≥30 ng/ml	
Gender	**Male**	10 (12.4)*	0 (0)	0.47
	Female	73 (87.95)	6 (100)	
BMI	**Overweight**	12 (14.45)	1 (16.66)	0.62
	Obese	71 (85.54)	5 (83.33)	
WC	**<80cm in women <94cm in men**	1 (1.2)	0 (0)	0.93
	≥ 80cm in women ≥ 94cm in men	82 (98.8)	6 (100)	
SBP	**<130**	75 (90.4)	3 (50)	0.023
	≥130	8 (9.6)	3 (50)	
DBP	**<85**	73 (87.95)	4 (66.66)	0.18
	≥85	10 (12.04)	2 (33.33)	
TG	**<150 mg/dl**	49 (59.04)	2 (33.33)	0.18
	≥150 mg/dl	34 (40.96)	4 (66.67)	
HDL	**<40mg/dl in men <50mg/dl in women**	26 (31.32)	2 (33.33)	0.71
	≥40mg/dl in men ≥ 50mg/dl in women	57 (68.68)	4 (66.67)	
FBS	**<100 mg/dl**	65 (78.31)	1(16.67)	0.013
	≥100 mg/dl	17 (21.69)	5(83.33)	
Metabolic syndrome	**Yes**	30(36.14)	4 (66.67)	0.15
	No	53 (63.86)	2 (33.33)	

*Count (percent)
fisher exact test

Table 3. Correlations between independent variables and levels of vitamin D

Independent variables	Correlation coefficient (r)	*P*
Age	0.33	0.001
Fasting blood sugar	0.29	0.007
HDL-C	0.14	0.22
Systolic blood pressure	0.22	0.03
Diastolic blood pressure	0.14	0.17
Triglyceride	0.07	0.51
Body mass index	0.04	0.70
Waist circumference	0.10	0.31

Table 4. Regression model for each of the independent variables

Independent variables	Regression	*P*
Age	0.06	0.40
Gender	19.26	0.99
Fasting blood sugar	0.03	0.59
HDL-C	0.51	0.94
Systolic blood pressure	0.20	0.09
Diastolic blood pressure	0.06	0.61
Triglyceride	0.00	0.96
Body mass index	0.03	0.83
Waist circumference	0.06	0.50

The overall regression equation
P=0.89

Discussion

This study showed high prevalence of vitamin D deficiency. There was no significant association between metabolic syndrome and vitamin D deficiency. Among the components of metabolic syndrome, thesignificant inverse correlation was found between vitamin D deficiency with FBS and also SBP.

Similar to our study, a high prevalence of vitamin D deficiency (93.6%) was found in a study conducted by Lu *et al.,* on adult population in China (8). This is reasonable due to the similar geographic and socioeconomic condition with our country. In a Study by Jose I.Botella, 50.7% of participants had vitamin D deficiency. This lower frequency is somewhat justified due to the definition of vitamin D deficiency, While our study is considered the lowercut off points (10).

No significant association was found between metabolic syndrome and vitamin D deficiency. The results of studies on the relationship between vitamin D level and components of the metabolic syndrome are contradictory. Our results are inconsistent with the results of Bonakdaran, Ford, and Reis which vitamin D level was significantly lower in patients with metabolic syndrome (11-13). Jared P.Reis. Observed inverse association of 25(OH) D with metabolic syndrome, independent of potential confounding factors such as calcium intake and PTH (13). In this study, an increased risk of metabolic syndrome with increased PTH levels was demonstrated among older men (13). In contrast to our study, Paknahad, Bonakdaran and also Brock observed an inverse association between vitamin D level and FBS (2,11,14). They have suggested increased insulin secretion, insulin sensitivity, stimulation of insulin receptor expression, transport of glucose into target tissues and intracellular calcium regulation as possible mechanisms for vitamin D function. The reason for paradox results between vitamin D deficiency and FBS and SBP (direct correlation) maybe due to small number of participants in this study and very low case of normal vitamin D level (Six persons) in our research. Although thehigh prevalence of vitamin D deficiency maybe the most important reason for this results.

Paknahad found no relationship between BP and vitamin D level (2). Meta-analysis of Burgaz *et al.,* from 18 studies including four prospective studies and fourteen cross-sectional studies showed that blood 25-hydroxy-vitamin D concentration is inversely associated with hypertension (15). Possible mechanisms of the effects of vitamin D on blood pressure are renin-angiotensin regulation and Inhibition of renin mRNA expression. Several mechanistic studies confirming negative regulation of the renin gene by calcitriol have been published by the group of Li, who showed that renin expression and plasma angiotensin II production were increased several-fold in vitamin D receptor-null (VDR-null) mice, leading to hypertension, cardiac hypertrophy, and increased water intake. In wild-type mice, inhibition of 1.25 dihydroxyvitamin -D3 synthesis also led to an increase in renin expression, whereas 1.25 dihydroxyvitamin -D3injection led to renin suppression (16).

Our result is contrary to the previous study where the plasma HDL-C levels had a direct relationship with vitamin D level (6-7). Also, we did not find any correlation between vitamin D deficiency and serum triglyceride that is in contrast with Park and co-worker study (17).

The definitive conclusion of this cross sectional study is very difficult due to the difference in age of populations, different seasons that study performed, small sample size and lack of adjustment for important confounding factors. Also, comparison of vitamin D deficiency group with normal vitamin D group (Six persons) is incorrect due to thehigh prevalence of vitamin D deficiency and small sample size. Limitation of this study mentioned above. In this regards, designing clinical trials with long term follow up seems necessary

to determine the exact role of vitamin D in metabolic syndrome.

In this study, however, no significant association between vitamin D deficiency and metabolic syndrome was found, but considering the role of vitamin D deficiency, metabolic syndrome and obesity on cardiovascular diseases, it is necessary to assess and diagnose vitamin D deficiency and components of metabolic syndrome in obese individuals. Also, further studies with large sample size of two groups (normal and low vitamin D deficiency) are necessary.

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