

Original Article

Dietary intake of vitamin D and metabolic syndrome after 3-year follow-up: Tehran lipid and glucose study

Sakineh Shab-Bidar^a, Firoozeh Hosseini-Esfahani^b, Hossein Delshad^b,
Golaleh Asghari^b, Parvin Mirmiran^{*c}, Fereidoun Azizi^d

^a Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran

^b Nutrition and Endocrine Research Center, Obesity Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

^c Department of Clinical Nutrition and Dietetics, Faculty of Nutrition Sciences and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran

^d Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

ABSTRACT

Article History

Received:

15/11/2014

Revised:

30/12/2014

Accepted:

11/01/2015

Keywords:

Vitamin D,
Metabolic
syndrome,
Adults,
Iran

Background: The aim of this study was to examine the association between dietary intakes of vitamin D and the metabolic syndrome (MetS) in Tehranian adults, Iran.

Methods: In this population-based prospective study, a sample of 2357 subjects, aged 20-74 years, who had completed a validated food frequency questionnaire, were studied. MetS was defined according to the modified guidelines of the National Cholesterol Education Program Adults Treatment Panel III.

Results: Median intakes of vitamin D were 1.5 and 1.6 $\mu\text{g}/\text{day}$ in men and women respectively. After adjustment for confounding factors, dietary vitamin D intake was inversely associated with fasting blood glucose ($\beta = -0.085$, $p = 0.004$) and waist circumference ($\beta = -0.065$, $p = 0.035$); these associations were attenuated following further adjustment for demographics, body mass index (BMI) and dietary factors ($\beta = -0.066$, $p = 0.030$) and ($\beta = -0.065$, $p = 0.044$), respectively. An association was observed between incidence of MetS and vitamin D intake (p trend = 0.040), independent of age, gender, smoking, physical activity; this association remained following further adjustment for BMI (p for trend = 0.044) and dietary factors (p for trend = 0.051).

Conclusion: Our findings suggest a significant inverse association between dietary vitamin D intake, MetS, and some of its components after controlling for confounding factors.

Citation: Shab-Bidar S, Hosseini-Esfahani F, Delshad H, Asghari G, Mirmiran P, Azizi F. **Dietary intake of vitamin D and metabolic syndrome after 3-year follow-up: Tehran lipid and glucose study.** *J Nutr Sci & Diet* 2015; 1(2): 71-9.

Corresponding author:

Parvin Mirmiran, Ph.D.

Address: Nutrition and Endocrine Research Center, Obesity Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, P.O. box: 19395-4763, Tehran, Iran.

Email: parvin.mirmiran@gmail.com

Introduction

A complex accumulation of metabolic abnormalities including hyperinsulinism, impaired glucose tolerance, hypertension, low high density lipoprotein cholesterol (HDL-c) and hypertriglyceridemia, termed the “metabolic syndrome” (MetS) have an obscure etiology [1].

A recent study in Tehran showed that this syndrome is highly prevalent in Tehranian adults, with an estimated prevalence in adults of over 30% [2] which is higher than those in most developed countries [3]. It is thought that genetic, metabolic and environmental factors including diet play an important role in the development of this syndrome [4].

Low vitamin D status has been associated with cardiometabolic disease in cross-sectional and prospective studies [5, 6]. Recently, meta-analysis of cross-sectional studies has shown lower odds for cardiovascular disease (CVD), MetS and Type 2 diabetes (T2D) in highest versus the lowest levels of serum vitamin D (51%, 33% and 55%, respectively) [7].

In addition to vitamin D status, dietary and supplemental vitamin D intakes have been inversely associated with CVD risk. Recently vitamin D intervention with fortified foods has shown improvements in metabolic, endothelial and inflammation biomarkers in T2D [7-9]. In cross-sectional studies, dietary vitamin D was inversely and significantly related to body mass index (BMI) [10] and the highest category of total vitamin D and calcium intakes had the lowest prevalence of each of the components of MetS, except triglyceride (TG) [11]. In a prospective study, consumption of more vitamin D plus calcium was associated with a lower risk of developing incident diabetes [12]. In contrast, these associations were not observed in some studies [11, 12]. Differences in findings were potentially attributed to different study designs, diet data-collection and the use of different cut-offs of vitamin D for analysis. Various populations including different age groups and races, with various dietary patterns could have different levels of risk for MetS. Therefore investigating the associations between nutrients and risk of MetS in different populations seems critical. The current study was hence undertaken to assess the relationship of dietary vitamin D intake, MetS and its surrogates, among Tehranians, aged 20-74 years old, in a 3 years follow-up Tehran Lipid and Glucose Study (TLGS). We hypothesized that the incidence of MetS and its components during follow-up study would be lower in participants with higher dietary intake of vitamin D.

Methods

Study population

This study was conducted within the framework of the TLGS, a prospective

community-based investigation, aimed at ascertaining the prevalence of non-communicable disease risk factors and developing a healthy to curtail these risk factors [13]. Briefly, this study is being conducted on a sample of residents under the coverage of three medical health centers in district 13 of Tehran, the capital city of Iran. These health centers were considered together for analysis, being similar in participant characteristics, including the prevalence of MetS risk factors [13]. The first phase of the TLGS began in March 1999 and data collection, at 3 year intervals, is ongoing.

A total of 12,523 individuals participated in the third follow-up survey of TLGS (2006-2008). The mean duration of the follow-up was approximately 3 years. Of a total of 12,523 subjects, aged 3 years and over, who completed the examinations during the third phase of TLGS, 4920 were randomly selected for completing the dietary assessment, based on age and sex groups. Randomization was done because of the cost and complexity of dietary data collection and because this process is time consuming. Finally, dietary data of 3462 subjects, who agreed to participate and completed the food frequency questionnaire (FFQ) were available. Characteristics of participants who completed the validated FFQ were similar to those of the total population in the third phase of TLGS [14].

After excluding subjects with diabetes or history of CVD or stroke (because of possible changes in diet), those with missed values of weight, height, biochemical data, those whose reported daily energy intakes outside the range of 800-4200 kcal/day, and those aged < 20 or > 70, finally the data of 2357 adults (1087 men and 1270 women) remained. Of the 2357 initial participants who attended the baseline examination, 554 subjects who had no follow-up information on dietary intakes were excluded. Then, participants with MetS or its risk factors at baseline were excluded from the analysis; eventually, analyses were conducted on the data of participants: totally 936 participants for the analysis of MetS, 1059 for abdominal obesity, 1114 for impaired fasting glucose, 807 for hypertriglyceridemia, 890 for low-HDL-c, and 1388 for hypertension.

Each subject provided written informed consent. The protocol of this study was approved by the research council of the Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences.

Assessment of anthropometric measures

While the subjects were minimally clothed and not wearing shoes, weight was measured with the use of digital scales and recorded to the nearest 100 g. Height was measured with a tape measure while the subjects were standing with shoulders in a normal position and not wearing shoes. BMI was calculated. Waist circumference was measured at the umbilical level with the use of an unstretched tape measure without any pressure to body surface. Measurements were recorded to the nearest 0.1 cm and waist-to-hip ratio was calculated [13].

Assessment of physical activity

Physical activity level was assessed using the Persian translated modifiable activity questionnaire (MAQ) [15].

The frequency and time spent on light, moderate, hard and very hard intensity activities according to the list of common activities of daily life over the past year were obtained. Physical activity levels were expressed as metabolic equivalent hours per week (METs hours/week). High reliability and relatively moderate validity have been reported for the Persian translated MAQ in Tehranian adults [16].

Assessment of dietary intake

Usual dietary intake was assessed with the use of a validated 168 item-semi quantitative FFQ [17]. The FFQ consisted of a list of foods with a standard serving size. Participants were asked to report their frequency of consumption of each food item during the previous year on a daily, weekly or monthly basis. Portion sizes of consumed foods were converted from household measures to grams per day [18].

The validity and reliability of the FFQ were assessed in a random sample (based on sex and age groups), by comparing the data from 2 FFQs completed 1-year apart and comparing the data from 2 FFQs and twelve 24 hour dietary recalls, respectively. The validity and reliability of the FFQ for dietary intakes were acceptable; the energy adjusted correlation coefficients between the FFQ and twelve 24 h dietary recalls for vitamin D were 0.63 and 0.43 and those between the two FFQs were 0.57 and 0.71 in men and women participants, respectively.

Since the Iranian food composition table (FCT) is incomplete, and has limited data on nutrient content of raw foods and beverages [19], foods and beverages were analyzed for their energy and nutrient content using the United

States Department of Agriculture (USDA FCT) [14, 20] however, the Iranian FCT was used for some dairy products (like Kashk), which are not listed in the USDA FCT. The average dietary data through follow-up was considered to take into account the variability over time.

Assessment of other variables

Blood pressure was measured twice after the participants sat for 15 minutes [21]. Additional demographic information about age, gender, smoking habits, and medical history was obtained with the use of validated questionnaires.

Biochemical measurement

Fasting blood samples were drawn after > 12 hours overnight fasting for the measurement of glucose and lipid concentration [13]. Fasting blood glucose (FBG) was measured with an enzymatic colorimetric method using glucose-oxidase. Serum triacylglycerol concentrations were assayed with the use of TG kits (Pars Azmoon, Inc., Tehran, Iran) adapted to the Selectra auto analyzer (Vital Scientific, Spankeren, Netherlands); HDL-c was measured after precipitation of the apolipoprotein B-containing lipoproteins with phosphotungstic acid. Monitoring of assay performance was done once every 20 tests, using lipid control serum, percinorm (normal range) and percipath (pathologic range) wherever applicable (Boehringer Mannheim, Germany; cat.no.1446070 for percinorm and 171778 for percipath). Lipid standard (Cfas, Boehringer Mannheim, Germany; cat.no.759350) was used to calibrate the selectra 2 auto-analyzer daily for laboratory analyses and all samples were analyzed when internal quality control met the acceptable criteria. Inter- and intra-assay coefficients of variation were 1.6 and 0.6% for all markers [22].

Definition of terms

MetS was determined according to the modified National Cholesterol Education Program/Adult Treatment Panel III definition [23]. Participants with three or more of the following conditions were typically defined as having the MetS: (1) TGs, ≥ 150 mg/dl, (2) HDL-c, < 40 mg/dl in men and < 50 mg/dl in women; (3) elevated blood pressure, $\geq 130/85$ mmHg, and (4) abnormal glucose homeostasis, FBG ≥ 110 mg/dl. We coded waist circumference (WC) according to the newly-introduced cut-off points

for Iranian adults (≥ 95 cm for both genders) [24].

Statistical analysis

In separate models, first-order interactions between sex and vitamin D intakes were entered to ascertain whether associations were similar between men and women. We calculated energy adjusted intakes of vitamin D, using the residual method as advised by Willett (1989), which is the most widely used method to obtain relative intakes, justifying its application here [25]. Multiple linear regressions were applied to assess the relationship between vitamin D intake, taken as a continuous explanatory variable, and the MetS components as response variable. Data on mean dietary intakes of vitamin D at baseline and year 3 was used in analysis. We also applied a logistic regression model to examine the association between vitamin D intake and the risk of MetS. For logistic regression, dietary vitamin D was categorized into quartiles (< 0.86 , $0.86-1.79$, $1.8-2.79$ and ≥ 2.8). Participants with dietary vitamin D < 0.86 were considered as the reference group. Analyses were adjusted for the confounding factors. Five models were used: the initial model was the crude model. In the second model, we adjusted for age (continuous), sex, smoking status (current, past, and never) and physical activity (METs h/week). The third multivariate model was further adjusted for BMI (continuous). To take into account the variation in BMI over the 3 years, the mean of BMI was used as a covariate at entry and at 3 years. To the fourth multivariate model we added dietary factors, including macronutrients, total fiber intake and calcium. P for trend reported for variables when indicated. SPSS software (version 16; SPSS Inc., Chicago IL.) was used for all statistical analyses

Results

The reported mean daily intake of vitamin D was 1.01 ± 1.2 $\mu\text{g/day/1000 kcal}$. Mean and \pm standard deviations of age and anthropometric measures as well as the distribution of subjects in whole population with regard to BMI, smoking and physical activity status is shown in table 1. Except for dietary intake and current smoking ($p < 0.001$), no significant differences were found in the baseline characteristics across categories vitamin D intake. Macronutrient intake was greater across quartiles of vitamin D (Table 2).

In multiple linear regressions at 3-year follow-up after adjusting for demographic, BMI and dietary factors, vitamin D intake was

significantly related to serum FBG ($\beta = -0.07$, $p = 0.030$), WC ($\beta = -0.06$, $p = 0.040$) (Table 3). Vitamin D intake did not relate significantly to TG ($\beta = -0.04$, $p = 0.250$) and systolic blood pressure ($\beta = -0.032$, $p = 0.280$), diastolic blood pressure ($\beta = -0.03$, $p = 0.330$) and HDL-c ($\beta = -0.006$, $p = 0.800$) after adjustment for confounding variables.

Table 1. General demographic and clinical features

Variables	Results
Age (years)	38.3 ± 11.2
Sex (M/F) (1087/1270)	396/540
Weight (kg)	70.3 ± 13.3
Body mass index (kg/m^2)	25.1 ± 4.0
Physical activity (METs h/wk)	37.4 ± 23.5
Fasting blood glucose (mg/dL)	70.2 ± 13.0
TGs (mg/dL)	119.3 ± 126.5
HDL-c (mg/dL)	48.9 ± 11.8
WC (cm)	89.1 ± 10.5
Diastolic blood pressure (mmHg)	107.3 ± 14.0
Systolic blood pressure (mmHg)	71.3 ± 10.0
Calcium intake (mg/day/kcal)	577.5 ± 143.3
Vitamin D intake ($\mu\text{g/day/1000 kcal}$)	1.0 ± 1.2
Energy intake (kcal/day)	2357 ± 709
Total fat intake (g/day)	78.3 ± 28.2
Protein intake (g/day)	86.7 ± 30.2
Carbohydrate intake (g/day)	346.8 ± 114.5
Fiber intake (g/day)	46.0 ± 24.7

Data presented as mean \pm standard deviation or percentage unless stated otherwise

BMI = Body mass index; WC = Waist circumference; HDL-c = High density lipoprotein cholesterol; MetS = Metabolic syndrome; TG = Triglyceride

Prevalence of new cases of MetS in TLGS participants was 8% ($n = 75$) during 3 years. Adjusted risk ratios (RR) of MetS in vitamin D quartiles are shown in table 4. The RRs of having MetS decreased significantly with increments of dietary vitamin D quartiles. As shown in table 4, an inverse association between dietary vitamin D intake and risk of developing MetS over 3 year remained after adjusting for age, sex, smoking status, physical activity (p for trend = 0.030). Adjustment for BMI did not change the relation (Table 4). Compared with subjects who consumed a mean of 0.44 μg vitamin D in quartile 1, incidence of MetS was 28% lower in subjects who consumed a mean of 2 μg vitamin D in quartile 4 (p for trend = 0.040). After additional adjustment for macronutrients (carbohydrate, fat, and protein), total fiber intake and calcium intake, risk of MetS remained stable. No significant interactions by sex were observed for the association of vitamin D intakes and metabolic risk factors.

Table 2. Selected characteristics across quartiles of vitamin D intake in Tehranian adults without metabolic syndrome (n = 936)

Vitamin D intake	Quartiles of dietary vitamin D				p
	Q1	Q2	Q3	Q4	
Range	< 0.86	0.86-1.79	1.8-2.79	≥ 2.8	
Women (%)	56.3	53	58.7	62.5	0.230
Age (years)	38.7 ± 11.0	36.5 ± 9.4	37.6 ± 10.7	37.0 ± 10.0	0.330
BMI (Kg/m ²)	25.0 ± 4.2	25.0 ± 4.1	25.1 ± 3.6	25.2 ± 3.8	0.920
Current smoking (%)	13	8	10	16	< 0.050
Physical activity (MET)	41.8 ± 57	39.4 ± 57	26.8 ± 38	40.0 ± 58	0.630
Fasting blood glucose (mg/dL)	91.6 ± 9.9	91.6 ± 13.0	91.0 ± 6.0	91.2 ± 12.6	0.930
TGs (mg/dL)	113 ± 59	130 ± 60	121 ± 72	113 ± 58	0.400
HDL cholesterol (mg/dL)	11.1 ± 0.73	11.0 ± 0.73	13.4 ± 0.89	11.5 ± 0.74	0.490
WC (cm)	89.0 ± 11.1	89.6 ± 11.2	88.6 ± 9.6	88.7 ± 9.9	0.540
Diastolic blood pressure (mmHg)	74.7 ± 10.8	74.6 ± 10.4	75.0 ± 9.6	76.2 ± 10.0	0.830
Systolic blood pressure (mmHg)	110 ± 17.2	110 ± 13.0	110 ± 12.5	110 ± 13.1	0.930
Calcium intake (mg/day/kcal)	534 ± 132	550 ± 139	602 ± 148	621 ± 134	< 0.001
Vitamin D intake (µg/day/kcal)	0.43 ± 0.24	0.70 ± 0.34	1.1 ± 0.42	1.8 ± 2.0	< 0.001
Energy intake (kcal/day)	2070 ± 641	2290 ± 672.8	2400 ± 714	2644 ± 693	< 0.001
Total fat intake (g/day)	66.5 ± 24.0	76.1 ± 25.4	78.9 ± 29.3	90.2 ± 28.6	< 0.001
Protein intake (g/day)	73.1 ± 26.0	81.2 ± 30.0	88.9 ± 27.1	102 ± 30.0	< 0.001
Carbohydrate intake (g/day)	310 ± 108	338 ± 114	353 ± 110	382 ± 115	< 0.001
Fiber intake (g/day)	41.0 ± 21.1	45.0 ± 22.4	46.6 ± 21.1	51.5 ± 31.6	< 0.001

Data presented as mean ± standard deviation or percentage unless stated otherwise p value obtained by ANOVA or chi-square between groups

BMI = Body mass index; WC = Waist circumference; HDL-c = High density lipoprotein cholesterol; MetS = Metabolic syndrome; TG= Triglyceride

Table 3. Multiple linear regression analysis of the association between dietary vitamin D intake and metabolic syndrome components over a 3 years follow-up: The Tehran Lipid Glucose Study

Outcome per unit increase in vitamin D intake (µg/1000 kcal)	Fasting glucose (mmol/l)	Fasting TG (mmol/l)	HDL cholesterol (mmol/l)	WC (cm)	Diastolic blood pressure (mmHg)	Systolic blood pressure (mmHg)
Model 1						
β	-0.085	-0.031	-0.01	-0.065	-0.069	-0.072
(95% CI)	-1.39 to 0.25	-1.97 to 0.75	-0.60 to 0.43	-0.99 to 0.037	-1.06 to 0.14	-1.4 to 0.22
p value	0.004	0.37	0.75	0.035	0.011	0.007
Model 2						
β	-0.063	-0.01	-0.025	-0.064	-0.048	-0.047
(95% CI)	-1.16 to 0.047	-1.45 to 1.09	-0.73 to 0.36	-0.84 to 0.13	-0.85 to 0.049	-1.08 to 0.056
p value	0.034	0.77	0.50	0.037	0.08	0.077
Model 3						
β	-0.066	-0.043	-0.006	-0.06	-0.032	-0.033
(95% CI)	-1.20 to 0.063	-2.18 to 0.58	-0.63 to 0.54	-0.82 to 0.09	-0.74 to 0.23	-0.96 to 0.23
p value	0.030	0.25	0.88	0.040	0.26	0.23
Model 4						
β	0.14	-0.036	-0.005	-0.034	-0.027	-0.036
(95% CI)	-1.67 to 0.078	-2.09 to 0.75	-0.66 to 0.55	-0.78 to 0.12	-0.86 to 0.26	-0.72 to 0.14
p value	0.031	0.350	0.890	0.044	0.300	0.180

Model 1: Crude β, Model 2: Adjusted for baseline outcome variables, age, sex, smoking status, physical activity, Model 3: Adjusted as in model 2 plus BM,; Model 4: Adjusted as in Model 3 plus macronutrient intake (carbohydrate, fat and protein), total fiber intake and calcium. Number of participants: 1059 for abdominal obesity, 1114 for impaired fasting glucose, 807 for hypertriglyceridemia, 890 for low-HDL-c, and 1388 for hypertension. CI= Confidence interval, WC= Waist circumference, HDL-c= High density lipoprotein cholesterol

Table 4. Adjusted risk ratio of MetS1 according to quartiles of dietary vitamin D intake over 3 years follow-up*: Tehran Lipid and Glucose Study

MetS	Vitamin D intake ($\mu\text{g/day}/1000 \text{ kcal}$)				p value
	Q1	Q2	Q3	Q4	
Model 1	1	1.13 (0.61 to 2.08)	0.40 (0.18 to 0.89)	0.61 (0.30 to 1.2)	0.038
Model 2	1	1.29 (0.66 to 2.52)	0.35 (0.13 to 0.93)	0.73 (0.32 to 1.62)	0.042
Model 3	1	1.29 (0.65 to 2.52)	0.35 (0.13 to 0.93)	0.72 (0.32 to 1.61)	0.044
Model 4	1	1.70 (1.06 to 2.73)	0.44 (0.22 to 0.88)	0.92 (0.52 to 1.65)	0.050
Model 5	1	1.05 (0.65 to 1.78)	0.61 (0.33 to 1.10)	1.40 (0.78 to 2.21)	0.340

Model 1: Crude RR, Model 2: Adjusted for baseline outcome variable, age, sex, smoking status, physical activity, Model 3: Adjusted as in model 2 plus BMI, Model 4: Adjusted as in Model 3 plus macronutrients intake (carbohydrate, fat and protein), total fiber intake and calcium, Model 5: Adjusted as in Model 4 excluding calcium plus dairy products. Dietary vitamin D was categorized into quartiles (< 0.86 , 0.86 - 1.79 , 1.79 - 2.79 and ≥ 2.8 , $\mu\text{g/day}/1000 \text{ kcal}$). Number of participants: totally 936 participants for the analysis of MetS. MetS = Metabolic syndrome, BMI = Body mass index

Discussion

In the TLGS, a prospective study with a 3-year follow-up, we observed an inverse association between some components of MetS (including WC and FBG) with vitamin D intake which remained after adjustments for possible cofounders. We also found that lower vitamin D intake was associated with risk of MetS. After adjustment for cofounders, this relationship remained significant.

Consistent with our results, in the British cohort study and NHANES III study, a lower prevalence of abdominal obesity was found with higher intake of vitamin D [11, 26]. In addition, an inverse relation was observed between dietary vitamin D intake and waist circumference in the Women's Health Study [11]. In a prospective study with a 20 year follow-up, 4727 black and white young men and women from the Coronary Artery Risk Development in Young Adults study, the intake of vitamin D from dietary and supplemental sources was inversely related to the 20 year cumulative prevalence of abdominal obesity ($p = 0.050$) [27].

The association of dietary vitamin D intake and FBG observed in our study is in agreement with other similar studies that indicate an inverse relation between the total vitamin D intake and prevalence of high glucose concentrations in young adults [27]. In US adult participants in the NHANES III, higher serum 25-hydroxyvitamin D (25(OH) D) concentrations were beneficially related to the insulin-sensitivity index [28] and glucose concentrations [11], respectively. In two prospective studies, a significant inverse relation between baseline serum 25(OH) D and incident high fasting glucose concentrations after 10 years of follow-up [29] and decreased risk of T2D with greater calcium and vitamin D intakes [30] were observed.

In this prospective cohort study, we observed

a significant inverse relation between prevalence of the MetS and vitamin D intake after taking into account potential cofounders. Our results are consistent with those obtained in the prospective study which showed 30% reduced odds for MetS for the highest quartile of dietary intake. However, median intake of vitamin D was only $0.81 \mu\text{g}/1000 \text{ kcal/day}$. The average daily vitamin D intake estimated from the dietary dataset was less than recommended values. In the current study, benefits from vitamin D were observed in individuals with vitamin D intakes $> 2.8 \mu\text{g}/1000 \text{ kcal/day}$ in whom the incidence of MetS was 28% lower. While, in the another study, risk of developing MetS was 18% lower in subjects who consumed an average of $20.58 \mu\text{g}$ vitamin D in quintile 5, compared with individuals who consumed an average of $2.47 \mu\text{g}$ vitamin D in quintile 1, (p trend = 0.030).

Our results also showed that the significant association between vitamin D and MetS was maintained after adjustment for calcium. Similar to our results, adjusted for calcium intakes in NHANES (2003-2004) data showed the association of vitamin D intakes with odds of having MetS [27].

Although attenuated, but still persistent the significant association after adjustment for BMI might imply both direct and indirect effects of vitamin D on MetS.

Confounding by sun exposure may have also influenced these results. In our study, we had inadequate measures of overall vitamin D intake due to the lack of information on sun exposure in the TLGS dataset. Even having such information on sun exposure does not help us to receive enough vitamin D, because geographically, Tehran which is situated at $35^{\circ}4'$ latitude, a polluted area, which plays a role in a vitamin D deficiency [31].

Only a few foods contain significant amounts of vitamin D. In general, cutaneous synthesis provides most of the vitamin D to the body (80-100%) [32]. Vitamin D-fortified milk products, certain types of fish, egg yolks, and other foods fortified with vitamin D, are more important because of recommendation for use of sunscreen and avoidance of direct sun exposure to prevent skin cancer. In Iran some rich sources are dairy products and fish; other important sources are meat and eggs, and we do not have foods fortified with vitamin D. In the US and western countries using fortified foods and supplements is common. These two factors apparently restrict intake of vitamin D.

It is noteworthy to keep in mind that associations between vitamin D intake with MetS and its components may be influenced by polymorphisms in vitamin D-binding proteins [33] or vitamin D receptor [34].

The underlying mechanisms by which vitamin D intake influences MetS are still not well understood, increase in circulating serum 25(OH) D suggests a rise in the body weight set point mechanism that explains associations between dietary vitamin D and risk of MetS [35]. Vitamin D intake may modulate the promotion of the influx of calcium in the regulation of insulin secretion and, therefore, the maintenance of glucose tolerance [36, 37].

To mention limitations of the current study first, endogenous vitamin D synthesis from sun exposure, which can be considerable, was not assessed as only 25(OH) D concentration reflects vitamin D synthesis from sun exposure. Second, we did not record any information on vitamin and mineral supplement use and alcohol consumption in our population; there are no official or unofficial data documented on alcohol consumption for Iranian populations, essentially because alcohol consumption is prohibited in Iran. Third, another limitation is that the USDA FCT was used for analyzing the energy and nutrients in foods, because we do not have an Iranian FCT. Fourth, subjects with known chronic artery disease, diabetes and stroke were excluded from the study. These exclusions may have reduced the likelihood of finding significant trends in odds of having MetS across quartile categories of our study parameters. In addition, chronic diseases such as MetS are heterogeneous and along with dietary patterns, other factors, such as heredity may need to be considered. Sixth, most of the risk factors are interrelated and could confound the relation

between dietary vitamin D and MetS risk. Since the design of our study was observational, the causative nature of associations cannot be determined. Classic adjustment for a wide range of confounding factors was done, but we cannot exclude confounding by factors we did not consider, or residual confounding by factors for which we did not adjust sufficiently. To find causality, there is a need for specifically designed dose-response randomized controlled trials or Mendelian genetic randomization studies.

However, our study does have several strengths including the prospective nature of the data, the use of a population-based sample, the large number of participants, the use of multiple linear regression models and adjustment of confounding variables in the association of dietary vitamin D with MetS.

Conclusion

We found that higher dietary vitamin D intake is associated with lower prevalence of the MetS, WC and FBG in Tehranian adults. However, future studies including adequately dose-response randomized trials of vitamin D supplementation or genetic Mendelian randomization approach should be addressed for the causal relationship.

Acknowledgments

We thank the participants in the TLGS for their enthusiastic support and the staff of the Research Institute for Endocrinology and Metabolism, TLGS Unit. None of the authors had any personal or financial conflicts of interest. We would like to thank Ms.N.Shiva for critical editing of English grammar and syntax of the manuscript.

Conflict of interest

None of the authors had any personal or financial conflicts of interest.

References

1. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes*. 1988; 37(12): 1595-607.
2. Azizi F, Emami H, Salehi P, Ghanbarian A, Mirmiran P, Mirbolooki M, et al. Cardiovascular risk factors in the elderly: the Tehran Lipid and Glucose Study. *J Cardiovasc Risk*. 2003; 10(1): 65-73.
3. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*. 2002; 287(3): 356-9.
4. Rennie KL, McCarthy N, Yazdgerdi S, Marmot M, Brunner E. Association of the metabolic

- syndrome with both vigorous and moderate physical activity. *Int J Epidemiol.* 2003; 32(4): 600-6.
5. Giovannucci E, Liu Y, Hollis BW, Rimm EB. 25-hydroxyvitamin D and risk of myocardial infarction in men: a prospective study. *Arch Intern Med.* 2008; 168(11): 1174-80.
 6. Heaney RP. Functional indices of vitamin D status and ramifications of vitamin D deficiency. *Am J Clin Nutr.* 2004; 80(6 Suppl): 1706S-9S.
 7. Parker J, Hashmi O, Dutton D, Mavrodaris A, Stranges S, Kandala NB, et al. Levels of vitamin D and cardiometabolic disorders: systematic review and meta-analysis. *Maturitas.* 2010; 65(3): 225-36.
 8. Shab-Bidar S, Neyestani TR, Djazayeri A, Eshraghian MR, Houshiarrad A, Gharavi A, et al. Regular consumption of vitamin D-fortified yogurt drink (Doogh) improved endothelial biomarkers in subjects with type 2 diabetes: a randomized double-blind clinical trial. *BMC Med.* 2011; 9: 125.
 9. Shab-Bidar S, Neyestani TR, Djazayeri A, Eshraghian MR, Houshiarrad A, Kalayi A, et al. Improvement of vitamin D status resulted in amelioration of biomarkers of systemic inflammation in the subjects with type 2 diabetes. *Diabetes Metab Res Rev.* 2012; 28(5): 424-30.
 10. Kamycheva E, Joakimsen RM, Jorde R. Intakes of calcium and vitamin d predict body mass index in the population of Northern Norway. *J Nutr.* 2003; 133(1): 102-6.
 11. Liu S, Song Y, Ford ES, Manson JE, Buring JE, Ridker PM. Dietary calcium, vitamin D, and the prevalence of metabolic syndrome in middle-aged and older U.S. women. *Diabetes Care.* 2005; 28(12): 2926-32.
 12. Pittas AG, Dawson-Hughes B, Li T, Van Dam RM, Willett WC, Manson JE, et al. Vitamin D and calcium intake in relation to type 2 diabetes in women. *Diabetes Care.* 2006; 29(3): 650-6.
 13. Azizi F, Rahmani M, Emami H, Mirmiran P, Hajipour R, Madjid M, et al. Cardiovascular risk factors in an Iranian urban population: Tehran lipid and glucose study (phase 1). *Soz Praventivmed.* 2002; 47(6): 408-26.
 14. Hosseini-Esfahani F, Jessri M, Mirmiran P, Bastan S, Azizi F. Adherence to dietary recommendations and risk of metabolic syndrome: Tehran Lipid and Glucose Study. *Metabolism.* 2010; 59(12): 1833-42.
 15. Kriska AM, Knowler WC, LaPorte RE, Drash AL, Wing RR, Blair SN, et al. Development of questionnaire to examine relationship of physical activity and diabetes in Pima Indians. *Diabetes Care.* 1990; 13(4): 401-11.
 16. Momenan AA, Delshad M, Sarbazi N, Rezaei GN, Ghanbarian A, Azizi F. Reliability and validity of the Modifiable Activity Questionnaire (MAQ) in an Iranian urban adult population. *Arch Iran Med.* 2012; 15(5): 279-82.
 17. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. *Public Health Nutr.* 2010; 13(5): 654-62.
 18. Ghaffarpour M, Houshyar-Rad A, Kianfar H. *The Manual for household measures, cooking yields factors and edible portion of food.* Tehran, Iran: Keshavarzi Press; 1999.
 19. Azar M. *Food composition table of Iran.* Tehran, Iran: National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences; 1980.
 20. Gannage-Yared MH, Azoury M, Mansour I, Baddoura R, Halaby G, Naaman R. Effects of a short-term calcium and vitamin D treatment on serum cytokines, bone markers, insulin and lipid concentrations in healthy post-menopausal women. *J Endocrinol Invest.* 2003; 26(8): 748-53.
 21. Azizi F, Ghanbarian A, Madjid M, Rahmani M. Distribution of blood pressure and prevalence of hypertension in Tehran adult population: Tehran Lipid and Glucose Study (TLGS), 1999-2000. *J Hum Hypertens.* 2002; 16(5): 305-12.
 22. Azizi F, Ghanbarian A, Momenan AA, Hadaegh F, Mirmiran P, Hedayati M, et al. Prevention of non-communicable disease in a population in nutrition transition: Tehran Lipid and Glucose Study phase II. *Trials.* 2009; 10: 5.
 23. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation.* 2009; 120(16): 1640-5.
 24. Azizi F, Hadaegh F, Khalili D, Esteghamati A, Hosseini-panah F, Delavari A, et al. Appropriate definition of metabolic syndrome among Iranian adults: report of the Iranian National Committee of Obesity. *Arch Iran Med.* 2010; 13(5): 426-8.
 25. Walter W. *Nutritional epidemiology.* 2nd ed. Oxford, UK: Oxford University press; 1989.
 26. Hypponen E, Boucher BJ, Berry DJ, Power C. 25-hydroxyvitamin D, IGF-1, and metabolic syndrome at 45 years of age: a cross-sectional study in the 1958 British Birth Cohort. *Diabetes.* 2008; 57(2): 298-305.
 27. Fung GJ, Steffen LM, Zhou X, Harnack L, Tang W, Lutsey PL, et al. Vitamin D intake is inversely related to risk of developing metabolic syndrome in African American and white men and women over 20 y: the Coronary Artery Risk Development in Young Adults study. *Am J Clin Nutr.* 2012; 96(1): 24-9.

28. Tai K, Need AG, Horowitz M, Chapman IM. Vitamin D, glucose, insulin, and insulin sensitivity. *Nutrition*. 2008; 24(3): 279-85.
29. Botella-Carretero JJ, Alvarez-Blasco F, Villafruela JJ, Balsa JA, Vazquez C, Escobar-Morreale HF. Vitamin D deficiency is associated with the metabolic syndrome in morbid obesity. *Clin Nutr*. 2007; 26(5): 573-80.
30. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985; 28(7): 412-9.
31. Hosseinpanah F, Pour SH, Heibatollahi M, Moghbel N, Asefzade S, Azizi F. The effects of air pollution on vitamin D status in healthy women: a cross sectional study. *BMC Public Health*. 2010; 10: 519.
32. DeLuca HF. Vitamin D: new horizons. *Clin Orthop Relat Res*. 1971; 78: 4-23.
33. Winters SJ, Chennubhatla R, Wang C, Miller JJ. Influence of obesity on vitamin D-binding protein and 25-hydroxy vitamin D levels in African American and white women. *Metabolism*. 2009; 58(4): 438-42.
34. Neyestani TR, Djazayeri A, Shab-Bidar S, Eshraghian MR, Kalayi A, Shariatzadeh N, et al. Vitamin D Receptor Fok-I polymorphism modulates diabetic host response to vitamin D intake: need for a nutrigenetic approach. *Diabetes Care*. 2013; 36(3): 550-6.
35. Foss YJ. Vitamin D deficiency is the cause of common obesity. *Med Hypotheses*. 2009; 72(3): 314-21.
36. Perez-Lopez FR. Vitamin D metabolism and cardiovascular risk factors in postmenopausal women. *Maturitas*. 2009; 62(3): 248-62.
37. Oh JY, Barrett-Connor E. Association between vitamin D receptor polymorphism and type 2 diabetes or metabolic syndrome in community-dwelling older adults: the Rancho Bernardo Study. *Metabolism*. 2002; 51(3): 356-9.