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Original Article



Association of Nutrient Patterns with Metabolic Syndrome and Its Components in Iranian Adults

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ABSTRACT

We aimed to examine the association between nutrient patterns and metabolic syndrome (MetS) in Iranian adults. In a cross-sectional study of 850 self-certified healthy women and men aged 20–59 years old, dietary data were assessed using three 24-hour recall. Anthropometric measures were done and blood samples were collected to measure serum fasting serum glucose and lipid profile. The MetS was defined using the International Diabetes Federation. Major nutrient patterns were identified using principle component analysis. In the first nutrient pattern, the individuals in the fifth quintile had a higher intake of vitamins B₁, B₂, B₃, B₅, B₆, B₁₂, zinc, iron, saturated fatty acids (SFAs), and protein. In the second nutrient pattern, individuals in the first quintile had lower consumption of zinc, SFAs, vitamin E, α -tocopherol, oleic acid, polyunsaturated fatty acids, β -carotene, linolenic acid, and monounsaturated fatty acids, compared to the fifth quintile. Furthermore, in the third nutrient pattern, the individuals in the fifth quintile had a higher intake of potassium, magnesium, phosphorous, calcium, protein, carbohydrate, vitamin C, and folate compared to other quintiles. We identified the second pattern had an indirect association with systolic and diastolic blood pressure, triglycerides, fasting blood sugar ($p < 0.001$ for all), and total cholesterol ($p = 0.04$) when it was controlled for body weight. Our findings showed that nutrient patterns may have an association with MetS components with mediating body weight.

Keywords: Diet; Nutrient patterns; Metabolic syndrome; Obesity

INTRODUCTION

Metabolic syndrome (MetS) is a multifarious problem which includes various factors [1]. Clinical conditions most commonly identified with MetS consist of insulin resistance, dyslipidemia (particularly high triglycerides (TGs), reduced high density lipoprotein [HDL] and low density lipoprotein [LDL]), visceral (abdominal) obesity, increased blood pressure, impaired glucose tolerance or diabetes mellitus, and high incidence of atherosclerotic disease [2]. Cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) are the

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Conflict of Interest

The authors declare that they have no competing interests.

culminating consequences of MetS which are used to characterize the most severe cases [3]. MetS is globally prevalent [1], but its exact prevalence varies according to the criteria applied, and often parallels the incidence of obesity and T2DM [4]. For example, in Iran, a national investigation in 2007 demonstrated a prevalence of MetS around 37.4%, according to the International Diabetes Federation (IDF) description, and 34.7% and 41.6% according to ATP III and ATP III/AHA/NHLBI standards, respectively. In Tunisia, another Middle Eastern country, the prevalence was reported to be 45.5% according to IDF standards, but based on ATP III thresholds, it was 24.3%. In addition, higher prevalence in women, compared to men, is routinely reported in Middle East countries [1]. The etiology of MetS consists of genetic, metabolic, and environmental factors [5], where dietary factors represent a significant feature in the pathology of MetS. In recent studies, dietary factors have been purported to represent parameters related to MetS [6]. However, there is a dearth of studies related to nutrient pattern versus food patterns [7]. It has been asserted that the easiest way to make public health advice is to use the results of food-based models [8]. Nevertheless, nutrient patterns research has various benefits, especially in an international research context. Firstly, nutrients are, predominantly, worldwide, functionally not interchangeable and, different from food patterns, may characterize particular nutritional profiles in an easier way to compare populations. Moreover, unlike foods, nutrients can reveal information on non-consumers [9]. Additionally, as compared to the use of food patterns, the nutrient pattern approach could better indicate a combination of bioactive nutrients in intricate biological mechanisms related with diseases [10].

Given the distinct lack of studies that have been conducted on the relationship between dietary nutrient patterns and MetS, the objective of our study was to investigate the association between nutrient patterns and MetS.

MATERIALS AND METHODS

Study design

This cross-sectional study was conducted among 850 apparently healthy individuals of both sex, aged 20–59 years old who referred to Health Human of Tehran medical center in 2017–2018. The sample size of 546 was calculated using this formula: $n = (pqz^2)/E^2$ considering where n = sample size; z^2 = square of the confidence level in standard error units (1.96); p = the estimate of the proportion of normal weight; $q = 1 - p$, or the estimated proportion of obese people; and E^2 = the square of the maximum allowance for error between the true proportion and the sample proportion (= 0.04). In order to compensate for the potential exclusion of participants due to under- and over-reporting of total energy intake, or attrition due to other reasons, the final sample size of 850 participants were selected for inclusion.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the ethical standards of the Tehran University of Medical Sciences (ethic number: IR.TUMS.VCR.REC.1398.429), who approved the protocol and informed consent form. All participants signed a written informed consent prior to the start of the study.

Eligibility criteria

Participants in this study were selected by a multistage cluster random sampling method from the 5 regions (north, south, east, west, and center) of Tehran. We selected multiple

health centers from each region and then we selected qualified individuals by easy sampling method from each health center. Participants with a history of diabetes, cancer, and CVD were excluded because of possible changes in their diet depending on their circumstances. Also people in the age range of 20 to 59 years old, apparently healthy individuals who willing to participate in our study, those who were members of the health center and living in Tehran were included.

Demographics

Additional covariates, including age, gender, smoking status (not smoking, quit smoking, low smoking), marital status (single, married, divorced, dead spouse), education status (illiterate, under diploma, diploma, educated), job status (employee, housekeeper, retired, unemployed), and physical activity level (low activity, moderate, vigorous) were obtained using validated questionnaires.

Assessment of dietary intake

The usual dietary intake of participants was assessed with three 24-hour recall questionnaires. The first 24-hour recall was collected by administered by a trained dietary interviewer during a face-to-face interview [11] and the other 2 recalls by a phone call to the participants on random days of the week. We extracted the meals and food groups from these questionnaires. The variables (total energy intake, crude, and energy-adjusted intake of all macronutrients) were included in the software. Macronutrients were also considered as a percentage of total caloric intake.

Identification of nutrient pattern

To identify nutrient patterns in our study population, the principal component analysis was used. Also we applied factor analysis with orthogonal transformation (varimax procedure) to derive nutrient patterns based on the 37 nutrients and bioactive compounds. The Bartlett test was significant at a p value less than 0.05, the Kaiser-Meyer-Olkin test was more than 0.6, and anti-image was more than 0.5, indicating that the correlation among the variables was sufficiently strong for factor analysis. Factors were retained for further analysis based on eigenvalues on the Scree test [12], then nutrient and their loading factors were stratified into 3 patterns by the type of nutrient patterns. In this study, we retained factors with eigenvalues > 3 as this cut off could result in more interpretable dietary patterns. In addition, factors with eigenvalues ≤ 3 did not explain sufficient amounts of overall variation. We computed the factor score for each nutrient pattern by summing up intakes of nutrients weighted by their factor loadings [12]. Each participant received a factor score for each identified pattern [13]. As simple linear dose-response relationships are unlikely to be found in nutritional epidemiology [13], we categorized the subjects based on quintiles of nutrient pattern scores.

Physical activity

Physical activity was assessed using the International Physical Activity Questionnaire (IPAQ), which is an interview-administered instrument. Based on the criteria, data were collected regarding walking, moderate, and vigorous activity, in the preceding week. In addition, time and frequency of activity days were recorded, and finally, a physical activity score was calculated. In the present study, we used the short form of the IPAQ (the "last 7 7-day recall" version of the IPAQ-Short Form), which records 3 intensity levels of activity based on the metabolic equivalents (METs). Finally, METs were classified as low (< 600 MET-minutes/week), moderate (600–3,000 MET-minutes/week), and vigorous ($> 3,000$ MET-minutes/week).

Assessment of anthropometric measurements

Anthropometric assessment included: weight, height, body mass index (BMI), waist circumference (WC), hip circumference (HC) and waist to hip ratio (WHR). Weight was measured by a digital scale with sensitivity of 0.1 kg (Seca808; Seca, Hamburg, Germany), while the subjects were minimally clothed and not wearing shoes. Height was measured while the subjects were standing, not wear shoes and shoulders were in a normal position. Height measurement by wall stadiometer with a sensitivity of 0.1 cm (Seca). BMI was calculated and expressed in kg/m². WC was measured at the midpoint between the last palpable rib and the iliac crest using a tape measure, during exhalation. To reduce subjective errors, all measurements were taken by the same technician.

Laboratory investigation

A blood sample was drawn about 10 mL between 7 am to 10 am from all study participants after they fasted overnight for 12 hours. After testing blood sample, people with a blood sugar above 126 mg/dL, individuals with history of diabetes and those taking blood sugar lowering medications, they are considered as diabetic patients. Total cholesterol (TC), TG, high density lipoprotein-cholesterol (HDL-C), fasting blood sugar (FBS) were measured using enzymatic methods, based on colorimetric assay, using commercial kits (Pars test, Iran) with an automatic device (Selectra E; Vitalab, Hoogerheide, The Netherland) for each patient. Individuals entered into the study with full explanations about this plan. Satisfaction was received from all patients to participate in this study and for blood sampling.

Metabolic syndrome (MetS)

The MetS was defined using the IDF: WC \geq 80 for women or \geq 94 cm for men in the presence of 2 or more of the following components: FBS \geq 100 mg/dL; systolic (or diastolic) blood pressure \geq 130 (or \geq 85) mmHg; HDL-C $<$ 50 mg/dL for women or $<$ 40 mg/dL for men; TG \geq 150 mg/dL [14].

Statistical methods

Characteristics of study participants were described using mean, standard deviation (SD), minimum, and maximum. Absolute nutrient intake was expressed in grams, milligrams and micrograms. Nutrient intakes adjusted for energy the calculated as the residual from the regression model, with absolute nutrient intake as the dependent variable and total energy intake as the independent variable [15]. As simple linear dose-response relationships are unlikely to be found in nutritional epidemiology [13], we categorized the subjects based on quintiles of nutrient pattern scores. Qualitative variables (gender, education, job-status, marriage, physical activity) were present as percent of number and p values obtained using χ^2 test. Assess components of MetS across quintiles of nutrient patterns' scores are presented as mean \pm SD with analysis of variance (ANOVA) test. Association between weight (mediation variable) with blood parameters and all of the patterns, mediation analyses were carried out to test the indirect effect of the weight on blood parameters.

We categorized the subjects based on quintiles of nutrient pattern scores. Quantitative and qualitative demographic variables were compared across quintiles of nutrient pattern scores using analysis of covariance and χ^2 tests, respectively.

Means of anthropometric measures across quintiles of nutrient pattern scores were calculated in for 2 genders. We used ANOVA test. To determine any association between nutrient patterns and MetS, with the adjustments, were calculated in different models for 2

genders. First model, unadjusted for any variable, In the second model, we further controlled for age, total energy intake and third model, additionally adjusted for current smoking, job status, education level and physical activity. All these analyses were done using binary logistic regression. Again, these analyses were done for both genders. In these analyses, the first quintile of the nutrient pattern scores was considered as the reference category. To compute the overall trend of odds ratios across increasing quintiles of nutrient pattern scores, we used the quintiles of each pattern in the logistic regression models.

Multiple mediation models (direct effect and indirect effect) of the relationship between the nutrient patterns, weight, and MetS with consider confidence interval 95 percent. All statistical analyses were performed using Statistical Package for Social Science (SPSS version 24.0; SPSS Inc., Chicago, IL, USA). Statistical significance was defined as $p \leq 0.05$.

RESULTS

Socioeconomic and clinical characteristics based on quintiles of the nutrient patterns are shown in **Supplementary Table 1**. The mean age of participants was 42 years. The mean BMI was 27 (overweight BMI classification). The mean blood pressure and lipid profile were in the normal range, whilst mean FBS was higher than the normal range.

We identified 3 major nutrient patterns. **Supplementary Table 2** details the principle factor loading of nutrient intake. The first pattern was characterized by a high factor loading of vitamins B₁, B₂, B₃, B₅, B₆, B₁₂, zinc, iron, saturated fatty acids (SFAs), and protein. The second pattern was characterized by a high factor loading of zinc, SFAs, vitamin E, α -tocopherol (α -TF), oleic acid, polyunsaturated fatty acids (PUFAs), β -carotene, linolenic acid (LA), monounsaturated fatty acids (MUFAs). The third pattern was characterized by a high factor loading of potassium, magnesium, phosphorus, calcium, protein, carbohydrate, vitamin C, and folate. These nutrient patterns represented 42% of variance explained in this population.

Supplementary Table 3 shows the nutrient intake based on quintiles of nutrient patterns. In the first nutrient pattern, the individuals in the fifth quintile had a higher intake of vitamins B₁, B₂, B₃, B₅, B₆, B₁₂, zinc, iron, SFAs, and protein. In the second nutrient pattern individuals in the first quintile had less consumption of zinc, SFAs, vitamin E, α -TF, oleic acid, PUFA, β -carotene, LA, MUFA compared to the fifth quintile. Furthermore, in the third nutrient pattern, the individuals in the fifth quintile had a higher intake of potassium, magnesium, phosphorous, calcium, protein, carbohydrate, vitamin C, folate compared to other quintiles.

Components of MetS based on gender and across quintiles of nutrient patterns are shown in **Table 1**. We observed a significant difference in FBS level ($p = 0.006$) across quintiles of first nutrient pattern in men. Moreover, we identified a significant difference for systolic blood pressure (SBP) and diastolic blood pressure (DBP) ($p = 0.02$) between quintiles in the first nutrient pattern in women. In the third nutrient pattern, we identified a significant association for SBP in women ($p = 0.02$). There were no significant differences between other components of MetS across quintiles of nutrient patterns.

Our findings showed that weight was associated with blood parameters and nutrient patterns (**Tables 2 and 3**). Of MetS components, there was no significant association between weight and HDL ($p = 0.18$). Also no association observed between weight and pattern 1 ($p = 0.41$)

Table 1. Components of metabolic syndrome across quintiles of nutrient patterns' scores

Characteristics	First nutrient pattern					Second nutrient pattern					Third nutrient pattern					
	Q1	Q3	Q5	p value	Q1	Q3	Q5	p value	Q1	Q3	Q5	p value	Q1	Q3	Q5	p value
Men																
Age (yr)	42.45 ± 13.77	44.39 ± 10.26	41.80 ± 11.34	0.89	44.23 ± 11.05	40.13 ± 10.22	45.04 ± 12.13	0.19	40.71 ± 14.09	42.74 ± 8.47	43.61 ± 10.47	0.83	40.71 ± 14.09	42.74 ± 8.47	43.61 ± 10.47	0.83
WC (cm)	89.55 ± 8.79	91.64 ± 15.45	93.97 ± 16.77	0.59	125.87 ± 21.09	118.43 ± 21.86	120.58 ± 29.70	0.72	87.03 ± 12.71	90.29 ± 15.17	94.68 ± 16.53	0.17	87.03 ± 12.71	90.29 ± 15.17	94.68 ± 16.53	0.17
SBP (mmHg)	124.25 ± 17.87	120.46 ± 30.43	127.56 ± 16.33	0.22	125.87 ± 21.09	118.43 ± 21.86	120.95 ± 29.70	0.61	125.03 ± 24.83	120.82 ± 24.37	122.59 ± 24.36	0.93	125.03 ± 24.83	120.82 ± 24.37	122.59 ± 24.36	0.93
DBP (mmHg)	75.75 ± 17.39	78.57 ± 22.00	83.86 ± 12.05	0.35	82.87 ± 16.84	79.00 ± 15.83	76.33 ± 17.96	0.55	83.00 ± 18.55	80.17 ± 14.79	79.97 ± 22.14	0.88	83.00 ± 18.55	80.17 ± 14.79	79.97 ± 22.14	0.88
FBS (mg/dL)	107.05 ± 37.41	109.36 ± 46.86	106.07 ± 23.30	0.006	109.81 ± 42.55	100.21 ± 12.79	116.67 ± 39.44	0.32	104.50 ± 31.39	104.79 ± 40.30	111.84 ± 27.80	0.76	104.50 ± 31.39	104.79 ± 40.30	111.84 ± 27.80	0.76
TG (mg/dL)	187.55 ± 128.57	180.71 ± 142.63	170.43 ± 87.99	0.51	171.58 ± 105.92	181.46 ± 89.15	192.96 ± 126.31	0.51	195.11 ± 142.97	162.62 ± 75.66	171.09 ± 91.17	0.74	195.11 ± 142.97	162.62 ± 75.66	171.09 ± 91.17	0.74
HDL (mg/dL)	41.60 ± 6.41	45.29 ± 8.11	45.15 ± 9.83	0.08	44.29 ± 8.25	45.72 ± 11.77	41.21 ± 5.13	0.13	44.36 ± 10.51	44.94 ± 7.34	45.25 ± 10.19	0.94	44.36 ± 10.51	44.94 ± 7.34	45.25 ± 10.19	0.94
Women																
Age (yr)	42.26 ± 10.80	41.21 ± 11.57	41.28 ± 11.00	0.20	42.24 ± 10.64	42.72 ± 10.67	41.68 ± 10.75	0.94	42.52 ± 11.24	44.23 ± 11.28	41.66 ± 10.99	0.17	42.52 ± 11.24	44.23 ± 11.28	41.66 ± 10.99	0.17
WC (cm)	88.12 ± 11.29	88.44 ± 10.59	86.87 ± 12.22	0.44	88.68 ± 11.48	90.00 ± 10.82	87.73 ± 11.70	0.15	87.81 ± 11.19	88.00 ± 11.24	87.88 ± 11.02	0.73	87.81 ± 11.19	88.00 ± 11.24	87.88 ± 11.02	0.73
SBP (mmHg)	118.10 ± 22.09	114.45 ± 19.73	112.63 ± 19.72	0.02	113.52 ± 20.58	116.33 ± 18.16	117.98 ± 18.24	0.06	110.58 ± 24.45	117.02 ± 16.51	116.71 ± 21.43	0.02	110.58 ± 24.45	117.02 ± 16.51	116.71 ± 21.43	0.02
DBP (mmHg)	79.05 ± 13.69	79.58 ± 14.36	77.70 ± 9.60	0.02	76.28 ± 12.21	78.66 ± 11.37	78.51 ± 12.74	0.30	77.14 ± 17.87	78.68 ± 12.11	78.80 ± 11.49	0.70	77.14 ± 17.87	78.68 ± 12.11	78.80 ± 11.49	0.70
FBS (mg/dL)	107.13 ± 27.01	111.06 ± 44.05	103.66 ± 26.80	0.56	113.37 ± 77.45	109.56 ± 36.96	108.21 ± 28.37	0.39	103.09 ± 25.63	107.63 ± 20.50	112.73 ± 75.80	0.39	103.09 ± 25.63	107.63 ± 20.50	112.73 ± 75.80	0.39
TG (mg/dL)	143.68 ± 78.27	134.01 ± 65.88	137.66 ± 65.96	0.84	127.43 ± 60.97	79.19 ± 148.95	142.46 ± 78.59	0.19	136.88 ± 73.71	139.41 ± 69.02	139.42 ± 71.55	0.57	136.88 ± 73.71	139.41 ± 69.02	139.42 ± 71.55	0.57
HDL (mg/dL)	49.67 ± 9.84	50.90 ± 8.79	51.50 ± 11.27	0.23	50.67 ± 9.69	52.10 ± 10.94	49.49 ± 10.02	0.15	52.18 ± 10.55	50.21 ± 8.95	51.86 ± 10.77	0.30	52.18 ± 10.55	50.21 ± 8.95	51.86 ± 10.77	0.30

Data are presented as mean ± standard deviation. The p obtained from analysis of variance test.

Q, quintile; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar; TG, triglycerides; HDL, high-density lipoprotein.

Table 2. Association between weight with blood parameters and all of patterns

Pattern and blood parameters	Coefficient	p value
SBP (mmHg)	0.03	< 0.001
DBP (mmHg)	0.03	< 0.001
TC (g/dL)	0.01	0.050
TG (g/dL)	0.02	< 0.001
HDL (mg/dL)	0.00	0.180
FBS (mg/dL)	0.01	< 0.001
Pattern 1	0.39	0.410
Pattern 2	-1.27	0.007
Pattern 3	0.84	0.070

SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL, high density lipoprotein; FBS, fast blood sugar.

and pattern 2 ($p = 0.07$) (**Table 2**). Because of the significant association of weight with blood parameters, mediation analyses were carried out to test the indirect associations of the weight on blood parameters, and weight was significantly associated with these markers as the mediator.

As shown in **Supplementary Figures 1-5**, the direct association between nutrient pattern 2 and SBP ($R = 0.07$; $p = 0.36$), DBP ($R = 0.11$; $p = 0.13$), TG ($R = 0.06$; $p = 0.39$), TC ($R = -0.10$; $p = 0.20$), and FBS ($R = 0.05$; $p = 0.43$) were not significant. Nutrient pattern 2 was significantly associated with body weight ($R = -1.27$; $p = 0.007$), and there was a significant association between body weight and SBP ($R = 0.03$; $p < 0.001$), DBP ($R = 0.03$; $p < 0.001$), TG ($R = 0.02$; $p < 0.001$), FBS ($R = 0.01$; $p < 0.001$) and TC ($R = 0.04$; $p = 0.04$). The second pattern shows an indirect association with SBP, DBP, TG, TC, and FBS when controlling for body weight. In **Supplementary Figure 6**, the direct association between nutrient pattern 1 and TG was not significant ($R = -0.03$; $p = 0.66$). No significant association was found between body weight and nutrient pattern 1 ($R = 0.84$; $p = 0.07$) and a significant association between body weight and TG ($R = 0.02$; $p < 0.001$).

Multivariate adjusted odds ratios and 95% confidence intervals for MetS by sex across quintiles of nutrient patterns are detailed in **Table 4**. No significant association was found between the 3 nutrient patterns and MetS was seen in men and neither in women. This non-significant association remained unchanged after adjusting for age, total energy intake, smoking, job status, education level, and physical activity.

Table 3. Multiple mediation models (direct effect and indirect effect) of the relationship between the nutrients pattern, weight, and metabolic syndrome

Variables	Pattern 1			Pattern 2			Pattern 3		
	Direct effect		Indirect effect Effect (95% CI)	Direct effect		Indirect effect Effect (95% CI)	Direct effect		Indirect effect Effect (95% CI)
	Coefficient	p value		Coefficient	p value		Coefficient	p value	
SBP (mmHg)	-0.17	0.25	0.01 (0.00, 0.10)	0.07	0.36	-0.04 (-0.07, -0.01)	0.07	0.38	0.02 (-0.08, 0.22)
DBP (mmHg)	0.02	0.75	0.01 (0.00, 0.11)	0.11	0.13	-0.04 (-0.08, -0.01)	0.05	0.47	0.05 (-0.09, 0.20)
TC (g/dL)	0.04	0.64	0.00 (0.00, 0.04)	0.10	0.20	-0.01 (-0.03, -0.00)	0.06	0.39	0.00 (0.00, 0.02)
TG (g/dL)	0.07	0.30	0.00 (0.00, 0.07)	0.06	0.39	-0.03 (-0.05, -0.01)	-0.03	0.66	0.02 (0.00, 0.04)
HDL (mg/dL)	-0.03	0.59	0.00 (0.00, 0.02)	-0.09	0.18	0.00 (-0.02, 0.00)	-0.02	0.75	0.00 (0.00, 0.02)
FBS (mg/dL)	-0.05	0.47	0.00 (0.01, 0.05)	0.05	0.43	-0.02 (-0.04, 0.00)	0.10	0.12	0.01 (0.00, 0.03)

CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL, high density lipoprotein; FBS, fasting blood sugar.

Table 4. OR (95% CI) for metabolic syndrome according to quintiles of nutrient patterns, stratified by gender

Characteristics	First nutrient pattern				Second nutrient pattern				Third nutrient pattern			
	Q1	Q3	Q5	p trend	Q1	Q3	Q5	p trend	Q1	Q3	Q5	p trend
Men												
Model 1	1.00	0.45 (0.14–1.46)	1.69 (0.57–4.95)	0.28	1.00	0.98 (0.42–2.30)	0.94 (0.31–2.25)	0.80	1.00	1.86 (0.67–5.14)	1.26 (0.48–3.26)	0.59
Model 2	1.00	0.38 (0.11–1.32)	1.64 (0.47–5.67)	0.52	1.00	1.11 (0.45–2.70)	0.72 (0.26–2.05)	0.56	1.00	1.10 (0.33–3.62)	0.47 (0.11–2.03)	0.26
Model 3	1.00	0.36 (0.10–1.29)	1.67 (0.46–5.99)	0.49	1.00	1.15 (0.46–2.86)	0.77 (0.25–2.36)	0.57	1.00	1.15 (0.34–3.90)	0.53 (0.12–2.36)	0.32
Women												
Model 1	1.00	1.03 (0.61–1.75)	0.79 (0.44–1.39)	0.38	1.00	1.37 (0.77–2.41)	1.09 (0.62–1.93)	0.92	1.00	1.27 (0.73–2.22)	1.31 (0.75–2.31)	0.50
Model 2	1.00	1.17 (0.66–2.06)	0.71 (0.38–1.33)	0.27	1.00	1.37 (0.75–2.50)	1.07 (0.58–1.99)	0.87	1.00	1.13 (0.60–2.14)	1.39 (0.64–2.99)	0.53
Model 3	1.00	1.19 (0.67–2.11)	0.71 (0.38–1.34)	0.25	1.00	1.39 (0.76–2.55)	1.13 (0.60–2.09)	0.93	1.00	1.10 (0.58–2.09)	1.30 (0.60–2.83)	0.73

Model 1: unadjusted; Model 2: age, total energy intake; Model 3: additionally adjusted for current smoking, job status, education level and physical activity. Q, quintile; OR, odds ratio; CI, confidence interval.

DISCUSSION

In the current study, we observed that the identified nutrient patterns were not associated with MetS. However, there were some associations between adherence to nutrient patterns and MetS components. Moreover, we found that the association between adherence to the second nutrient pattern and MetS components was mediated by body weight.

The second nutrient pattern was characterized by a high loading of vitamin E, α -TF, β -carotene, and unsaturated fatty acids, such as oleic acid and PUFAs. The relevance of vitamin E and MetS was assessed by Alcalá et al. [16], and they reported that obese mice fed on a high-fat diet, with 150 mg/kg of α -TF supplementation twice weekly, enhanced insulin sensitivity and hypertriglyceridemia, which was attributed to the decline of oxidative stress and inflammatory response. Vitamin E has been shown to have anti-inflammatory [17], anti-oxidative [18,19], and anti-hypercholesterolemic [20,21] features through regulation of different signaling pathways [22]. MetS is an inflammatory disease that also involves oxidative stress, thus, it is posited that vitamin E may have protective effects on MetS.

A previous study revealed that MetS patients had impaired absorption of dietary vitamin E, compared to healthy participants [23]. Additionally, in a randomized, double blind, placebo-controlled trial on patients with MetS, tocotrienol supplementation decreased TC, LDL-cholesterol, and HDL-C in subjects, in comparison to baseline [24]. Serum levels of α -TF have been positively linked to central obesity (defined as WC and WHR), but BMI may only be related to α -TF in men [25]. In contrast to our results, Barzegar-Amini et al. [26] concluded that serum vitamin E is negatively associated with WC and HC; although the reduction observed in body weight was not significant.

ω -3 and ω -6 FA PUFAs were inversely associated with MetS prevalence in females [27]; whilst greater total PUFA, and its sub-types (LA or α -LA), intake was negatively associated with hypertension and positively associated with abdominal obesity in a systematic review [28]. Some evidence from observational and interventional studies is in agreement with our results, where the benefits of both ω -3 and ω -6 PUFA in decreasing the odds of MetS [29–32] was evident. However, contrary results also exist [33–35].

Increased eicosapentaenoic acid (EPA) levels can significantly reduce interleukin (IL)-6 and other adipokine levels, including EPA, impeded nuclear factor- κ B (NF- κ B), a pro-inflammatory transcription factor, in comparison with a control group. Moreover, EPA can

elicit reductions in tumor necrosis factor- α (TNF- α), and further reduce its secretion in the presence of an NF- κ B inhibitor. This highlights the anti-inflammatory impact of ω -3 PUFAs and their beneficial effects in adipocyte inflammation and metabolic disorders, such as MetS [36]. It is noteworthy that the optimum dietary ratios of ω -6/ ω -3 PUFA of 1/1 and 5/1 can, evidently, diminish the lipid metabolism-related gene expression, and also significantly block the expression of the inflammatory cytokines IL-1, TNF- α and IL-6 [37].

The sufficient intake of MUFA and PUFAs in the Prevención con Dieta Mediterránea (PREDIMED) study, mostly due to high ingestion of nuts and olive oil, has been putatively related to the high adherence to Mediterranean diets (MedDiet) [38], and to a lower risk of CVD [39]. Moreover, other dietary pattern score approaches to stop hypertension, new Nordic, and vegetarian diets have also been suggested as substitutions to the MedDiet, as viable alternatives to prevent or reduce MetS occurrence [40].

Low-fat diets are generally reported to elicit decreases in body weight and/or WC, independently of fatty acid consumption [41,42]. Low-fat diets contain sufficient amounts of PUFA, or substituted by healthy sources of fats (fish, avocado, nuts, broccoli, thistle, olives, linseed and canola oil, etc.), or healthy sources of carbohydrate (whole grains, legumes, vegetables, and fruits), to elicit reductions in TG levels [41-44].

The diet rich in carotenes (particularly β -carotene) is found to be inversely associated with MetS and its components, which can be attributed to beneficial impacts on glucose metabolism [45]. In another study [46], intakes of dietary α -carotene, β -carotene, and lycopene conferred favorable effects on glucose metabolism in individuals at high risk for T2DM.

One of the strengths of our study is the usage of a validated food frequency questionnaire and adjustment for potential confounders in the analyses. However, some degree of measurement error is inevitable. Furthermore, trained dietitians were recruited to gather the food frequency data via interview; it is likely that this approach (as compared with self-administration) reduced any possible misclassification error. However, some limitations exist. This study was cross-sectional in design; thus, causal inferences cannot be concluded. Although the factor analysis method is identified to represent real-world dietary behaviors [47], this approach is founded on some subjective decisions such as naming nutrient patterns, method of rotation, and selection of food groups, which can trigger an overall assessment bias, but, it is helpful for us to have better understanding of diet-disease relations [48]. Another bias seen in some articles [49,50] is about the gender of participants. The reasons for the observed gender discrepancy in the associations between nutrient patterns with MetS are not understood, but it can be at least due to the differential effects of gonadal steroids on body composition and appetite. Also, behavioral, sociocultural and genetic factors may be part of the cause. Differences in the accuracy of dietary assessment among females and males could be another reason for this inconsistency. Our results are just limited to adults and other age ranges are not involved but because of enough sample size and method which is used for data collection, the power of study seems to be good for judgment.

CONCLUSION

In conclusion, the intake of the high amount of vitamin E, α -TF, β -carotene, and unsaturated fatty acids, such as oleic acid and PUFAs, is inversely associated with MetS components which

was mediated by body weight. Finally, the authors assert that prospective and high-quality clinical trial studies are necessary to explain the possible causal relationship of this result.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1

Characteristics of the investigating subjects

[Click here to view](#)

Supplementary Table 2

Principal factor loading of nutrients intake

[Click here to view](#)

Supplementary Table 3

Nutrient intakes across quintiles of nutrient patterns' scores

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Supplementary Figure 1

Multiple mediation models of the relationship between the second pattern, weight, and SBP.

[Click here to view](#)

Supplementary Figure 2

Multiple mediation models of the relationship between the second pattern, weight, and DBP.

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Supplementary Figure 3

Multiple mediation models of the relationship between the second pattern, weight, and TG.

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Supplementary Figure 4

Multiple mediation models of the relationship between the second pattern, weight, and TC.

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Supplementary Figure 5

Multiple mediation models of the relationship between the second pattern, weight, and FBS.

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Supplementary Figure 6

Multiple mediation models of the relationship between the first pattern, weight, and TG.

[Click here to view](#)

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