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The Association between Nutrient Patterns and Polycystic Ovary Syndrome: A Case-Control Study

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a common endocrine abnormality among reproductive-aged women. This study aimed to investigate the relevance of major nutrient patterns and PCOS. **Methods:** This age-body mass index (BMI) matched case-control study was conducted among 216 women with and without PCOS. The validated 178-items food frequency questionnaire (FFQ) was used for driving nutrient patterns. Logistic regression was used to assess the relationship between nutrient patterns and odds of PCOS. **Results:** Four major nutrient patterns were identified (65% of the variances of nutrient intake), including factor 1) high in carbohydrate, saturated fatty acids (SFA), total fat, and low in Eicosapentaenoic acid (EPA), Docosahexaenoic acid (DHA), factor 2) high loadings of SFA, cholesterol, vitamin D, total fat, and total fiber, factor 3) high in total fiber, EPA, DHA, chrome, vitamin C, vitamin D, and polyunsaturated fatty acids (PUFA), and factor 4) high loaded by fat, sodium, SFA, and low in vitamin D. Factor 1 and factor 4 nutrient patterns significantly increased the odds of PCOS (OR = 7.42; 95% CI 2.86, 18.1; P_{trend} < 0.001) and (OR = 11.32; 95% CI 4.3, 29.97; P_{trend} < 0.001), respectively. Also, the moderate adherence to factor 3 nutrient pattern had a protective effect on odds of PCOS (OR = 0.77; 95% CI 0.39, 0.98; P_{trend} = 0.04). **Conclusion:** It was found that factor 1 nutrient pattern increased the odds of PCOS and factor 3 nutrient pattern decreased the risk of PCOS. More prospective studies are required to confirm the study findings.

Keywords: *Nutrient pattern; Polycystic ovary syndrome; Factor analysis; Diet*

Introduction

Polycystic ovary syndrome (PCOS) is a multifactorial disorder with a complex of heterogeneous and heritable endocrine abnormalities among reproductive-age women (Goodarzi and Azziz, 2006, Norman *et al.*, 2007, Palomba *et al.*, 2015b). The prevalence of PCOS has been reported

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19.5% in Iran (Jalilian *et al.*, 2015a) and 15-20% worldwide (Sirmans and Pate, 2014). The Rotterdam criteria are commonly used to evaluate the prevalence of PCOS today (Jalilian *et al.*, 2015b). Infertility is one of the main complications of PCOS (Hull, 1987, Norman *et al.*, 2007). Also, it can cause endometrial carcinoma, anxiety, sleep apnea, and metabolic disorders, such as obesity, insulin resistance, type 2 diabetes, metabolic syndrome, hypertension, and cardiovascular diseases, if left untreated (Goodarzi *et al.*, 2011, Hardiman *et al.*, 2003, Palomba *et al.*, 2015a, Pastore *et al.*, 2011, Wang *et al.*, 2011). Although the etiology of PCOS is still unclear, it is considered as interactions between a complex genetic disorder and environmental factors, such as diet (Barber and Franks, 2013, Norman and Moran, 2007). Therefore, diet management has been suggested as a modifiable factor for improving PCOS (Teede *et al.*, 2011).

Long-standing studies have demonstrated an association between PCOS and nutrients, foods or food groups, or other different aspects of diets. These studies have suggested that carbohydrates with a low glycemic index and low-calorie diet (Turner-McGrievy *et al.*, 2014), and diet with high protein and low glycemic load (Mehrabani *et al.*, 2012), could be used for PCOS improvement . Also, some studies have estimated the effect of single nutrients, such as magnesium and selenium (Faghfoori *et al.*, 2017), magnesium and vitamin E co-supplementation (Shokrpour and Asemi, 2019), chromium (Amr and Abdel-Rahim, 2015, Fazelian *et al.*, 2017, Jamilian and Asemi, 2015), co-utilization of vitamin D and calcium (Asemi *et al.*, 2015, dehghani Firouzabadi *et al.*, 2012, Panjeshahin *et al.*, 2019), zinc (Foroozanfard *et al.*, 2015, Jamilian *et al.*, 2016), consumption of fiber (Faghfoori *et al.*, 2017), and omega-3 (Mohammadi *et al.*, 2012, Sadeghi *et al.*, 2017) on PCOS improvement . However, due to the presence of several nutrients in foods and their possible interactions, the evaluation of nutrients individually, cannot accurately show the association between nutrients and diseases, such as PCOS (Hu, 2002). The nutrient pattern approach, as a new direction in nutritional epidemiology, provides an evaluation of combined effects or interaction of nutrients or foods (Eslamian *et al.*, 2017), which might be different from the effects of each nutrient separately and could be more efficient to reduce chronic diseases. Some studies have associated the intake of macronutrients in PCOS women (Lin *et al.*, 2019, Moran *et al.*, 2013); however, the effects of macronutrients on odds of PCOS have not been measured as a nutrient pattern.

Dietary and nutrient patterns can be investigated in two ways (Kastorini *et al.*, 2013). A priori patterns that use diet indexevaluate adherence to a specific diet, such as the DASH diet, which its beneficial effects on PCOS (Asemi and Esmaillzadeh, 2015, Asemi *et al.*, 2014a, Azadi-Yazdi *et al.*, 2016, 2017, Foroozanfard *et al.*, 2017) have been shown. In contrast, posteriori patterns (data-driven methods) use exploratory statistical methods by summarizing the whole dietary intake into a few representative profiles. Although nutrients have previously been found to have a beneficial effect on PCOS, the relationship between nutrient patterns and PCOS has not been evaluated, since most studies have been done in the area of dietary pattern whether priori or posteriori (Ahmadi *et al.*, 2013, Asemi *et al.*, 2014b, Azadi-Yazdi *et al.*, 2016, Huijgen *et al.*, 2017, Moran *et al.*, 2015, Panjeshahin *et al.*, 2020, Panjeshahin *et al.*, 2019).

Therefore, due to the lack of studies on the relationship between major nutrient patterns derived from the posteriori approach and PCOS, the present study aimed to evaluate the association between major nutrient patterns and PCOS by using factor analysis among Iranian women.

Materials and Methods

Study design and participants: This age and body mass index (BMI) matched case-control study was conducted on women with and without PCOS, to evaluate the association between major nutrient

patterns and the odds of PCOS. The study participants contained women who referred to "Yazd Diabetes Clinic" and "Khatam clinic in Yazd", Iran; from January 2018 to March 2019. Also, some participants who had the inclusion criteria were introduced by endocrinologists from different parts of the city (multiple clinics) to obtain more satisfactory and academic data. The women were diagnosed with PCOS based on the standard Rotterdam criteria (ESHRE The Rotterdam ASRM-Sponsored PCOS Consensus Workshop Group, 2004). The participant's recruitment procedures are represented in **Figure 1**.

Diagnostic criteria suggested by Rotterdam (that is commonly used to evaluate the prevalence of PCOs) include the presence of at least two out of three diagnostic criteria, including (i) menstrual irregularities; (ii) clinical and/or biochemical signs of hyperandrogenism; (iii) abnormal ovarian ultrasound with ≥ 12 follicles in each ovary having a diameter of 2 – 9 mm or increased ovarian volume more than 10 cm^3 (Farshchi *et al.*, 2007, Jalilian *et al.*, 2015b). The case group included PCOS women diagnosed by the endocrinologist as a new patient (incident case). Women who did not have any symptoms of PCOS (based on Rotterdam criteria) were selected as the control group, who were companions of patients referring to other parts of the same clinic, or hospital, such as orthopedics, dentistry, optometry, etc.

Two groups were matched for age and BMI, using a frequency matching method. The inclusion criteria for the case group included females in reproductive age were diagnosed as a new case in PCOS (incidence case), subjects with no history of diseases, such as hyperprolactinemia, Cushing's syndrome, hypothyroidism, congenital adrenal hyperplasia, food allergy (so that some foods are not consumed(, not recently taken medications, such as contraceptive pills or hormonal drugs or other medications that could change the density of androgens, without type 1 diabetes, no alcohol consumption, no smoking, and lack of a special diet over the past year. Considering the difference between the mean PUFA in the two groups, and a 10% probability of sample loss, the minimum required sample size was calculated to be 108 women in each group.

Sample size calculation: Due to the limited number of similar articles, the appropriate reference for determining the sample size, considering alpha of 0.05 and a power of 90%, assuming that there is a 20% difference in adherence to dietary patterns in the two groups (P1 = 40%, P2 = 60%), and a 10% probability of sample loss, the minimum required sample size was calculated to be 108 women in each group.

P1 = the ratio of people who followed the dominant dietary pattern among the women without PCOS

P2 = the ratio of people who followed the dominant dietary pattern among the women with PCOS.

$$n = \frac{\left(Z_{1-a/2}\sqrt{2PQ} + Z_{1-\beta}\sqrt{P_1Q_1 + P_2Q_2}\right)^2}{(P_1 - Q_1)^2}$$

$$where\ P = \frac{P_1 + P_2}{2},\quad Q = 1 - P,$$

$$Q_1 = 1 - P_1\ and\quad Q_2 = 1 - P_2$$

Anthropometric measurements: All of the anthropometric indices were measured in a fasting condition by standardized methods. Height was measured using a non-stretched wall-mounted tape measure (to the nearest 0.1 cm) without shoes, standing, and in a normal position of shoulders status. Bodyweight and composition, such as body fat and body muscle percentage, and visceral fat were assessed using an Omron digital scale (model BF-511) to the nearest 0.1 kg, without shoes, and with minimal clothing. BMI was measured as weight (kg)/height (m^2). Waist circumference (WC) was recorded using a non-elastic tape measure (to the nearest 0.5 cm) placed approximately between the lower rib and iliac crest in a standing position. Also, hip circumference (HC) was measured using a non-elastic tape measure (to the nearest 0.5 cm) over the

widest part of the buttocks. WHR was calculated as WC (cm)/HC (cm). Body composition was recorded using a body composition analyzer (Omron model BF-511). All of these measurements were conducted by a trained investigator.

Blood pressure assessment: Blood pressure was measured using a standard mercury barometric device (Calibrated by the Iranian Institute of Standards and Industrial Research) after the subjects rested for five minutes in the seated position.

Physical activity assessment: The International Physical Activity Questionnaire-Short Form (IPAQ-SH) was used to measure physical activity data (Lee *et al.*, 2011). By summing both the frequency (days per week) and duration (minutes per day) for each type of activity, in categories of walking, moderate-intensity, and vigorous-intensity physical activity,physical activity was calculated. The metabolic equivalent value (MET) for each category is (walking minutes * 3.3 METs), (moderate-intensity physical activity minutes * 4.0 METs), (vigorous-intensity physical activity minutes * 8.0 METs). The score of each type of activity is MET of activity * minutes * days. The score of each type of activity must be gathered to express the total score of activity (Met-minutes/week).

Assessment of other covariates: The required information, such as age, demographic information, and socioeconomic status (SE) was collected using validated self-administered questionnaires. SE was evaluated based on home status (the owner/tenant), occupation and financial status (not satisfactory, satisfactory, and good), and family size (≤ 4, > 4 people), and education level (academic and non-academic education). If participants had ≤4 family members, satisfactory, and good status, were academically educated, and owned a house, they were given a score of 1 for each item. Then a total score was calculated. Other required variables, such as allergic to special foods (yes/no), history of adherence to a special diet over the last year (yes/no), marital status (married, single, widowed, and divorced), pregnancy history (yes/no), chronic diseases (hypertension, diabetes, stroke, cardiovascular diseases, and cancers) (yes/no), drug use for PCOS (yes/no), and whether their mother or sisters had a history of PCOS (yes/no), were evaluated using a validated self-administered questionnaire.

Dietary intake assessment: Common dietary intake of the recent year of each participant was measured by a 178-item semi-quantitative food frequency questionnaire (FFQ) with 551 questions. This FFQ was an adjusted model of a previously validated 168-item FFQ (Esfahani *et al.*, 2010), which was validated in the Tehran Lipid and Glucose Study (TLGS) (Azizi *et al.*, 2009). Ten additional questions related to the consumption of Yazd-specific food items frequently were added to the original 168-item FFQ. Also, the individuals participated in an interview by a questionnaire about the frequency of using supplements, including fish oil (or omega-3), calcium, vitamin D, folic acid, iron, and multivitamin-mineral supplements. The frequency response for food consumption had ten categories, including never or < 1 time/month, 1–3 times/month, 1 time/week, 2–4 times/week, 5–6 times/week, 1 time/day, 2–4 times/day, 5–7 times/day, 7–9 times/day, and 10 times or more/day. Face to face interview with the subjects was conducted by a dietitian who was blinded, to fill out all of the questionnaires. To increase the precision and accuracy of estimates, the portion sizes and the intake frequency of each food and beverage item, on average, were questioned. Then, the frequency was changed to daily consumption, and portion sizes were converted to the gram, using household measurements. Finally, the actual food intake (g/day) was transferred to Nutritionist IV to compute the total energy and nutrient intake. Eventually, total energy and nutrient intake were investigated by transferring food intake (g/day) to Nutritionist IV. One hundred and eighty-seven food items were

classified into 28 nutrient groups for nutrient pattern analysis. The specific groups were determined based on the similarity of nutrients items. Besides, each nutrient item was included just in one group.

Ethical consideration: Each participant provided a signed written informed consent after explaining the process of the study. The Human Research Ethics Committees of Shahid Sadoughi University of Yazd Medical Sciences approved the study protocol (IR.SSU.SPH.REC.1396.168).

Data analysis: Factor analysis with principal component analysis (PCA) as an extraction method was used to investigate the major nutrient patterns based on the twenty-eight nutrient groups. The eigenvalues > 1 and the scree plot in conjunction with the natural commentary of the factors identified whether a factor should be retained. Then factors (nutrient patterns) were rotated by varimax rotation (orthogonal). The originated factors were named based on the interpretation of the data from loaded factors of nutrient groups in each nutrient pattern (factor loading > 0.2), and the earlier literature. The summing of nutrient groups intake is weighted by their factor loadings and each participant gets a factor score for each identified pattern, conducted for evaluation of factor scores. The independent t-test was applied for comparing quantitative variables between cases and controls, whereas chi-square (χ^2 test) was used for categorical variables. Kolmogorov–Smirnov test was conducted to examine whether or not the distribution of variables is normal. Mean ± SD was presented for continuous variables, while qualitative variables used frequency (percentage). The characteristics of the participants were compared (by classification in quartiles) in the lowest and highest quartiles of the four nutrient scores using descriptive statistics. One-way ANOVA was used to compare general characteristics of quantitative variables across quartiles of nutrient patterns, and χ^2 tests were used for categorical variables. Odds Ratio (OR) and 95% confidence interval (CI) for crude and adjusted models were calculated. Multivariable logistic regression in different models were used to discover the relationship between nutrient patterns and PCOS. In model 1, the total energy intake was adjusted. In model 2, education, disease history, socioeconomic, diet history, marital status, pregnancy history, physical activity, and body fat percentage were added to the total energy intake. In model 3, visceral fat was added to previous adjustments in model 2. Also, in model 4, the total energy intake, education, disease history, socioeconomic, diet history, marital status, pregnancy history, physical activity, and WHR were adjusted. In all of the analyses, the first quartile of nutrient pattern scores was considered as a reference. To assess the overall trend of odds ratios across increasing quartiles of nutrient pattern scores, the quartile categories were treated as an ordinal variable in the analyses. All analyses were conducted using the statistical software IBM SPSS version 24 (IBM Corporation, Armonk, NY, USA)". P-values < 0.05 were considered statistically significant.

Results

Characteristics of the study population: Participant characteristics, energy intake, and physical activity of women with and without PCOS are reported in **Table 1**. The mean WC, WHR, fasting blood glucose (FBG), and visceral fat were significantly higher in the case group in comparison with the control group ($P < 0.05$). Also, in the case group, the mean energy intake was significantly higher, and the mean value of physical activity was significantly lower than the control group ($P < 0.001$). Moreover, no significant difference was observed in weight, HC, body muscle percentage, body fat percentage, socioeconomic status, pregnancy history, and socioeconomic and marital status were found between case and control groups.

Four major nutrient patterns were identified explaining a total 67.95% variance, using Factor analysis and Principal Component Analysis (PCA). These nutrient patterns included (A) "factor 1" high in carbohydrate, potassium, vitamin B (complex B1,

B2, B3, B5, B6, Biotin, B9, and B12), saturated fatty acids (SFA), fat, and low in eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and iron; (B) "factor 2" highly loaded with phosphor, SFA, calcium, cholesterol, vitamin D, fat, and total fiber; (C) "factor 3" consisting mainly of total fiber, EPA, DHA, chrome, vitamin C, potassium, iron, vitamin D, and polyunsaturated fatty acids (PUFA); (D) "factor 4" high in monounsaturated fatty acids (MUFA), fat, sodium, SFA, and low in vitamin D, vitamin k, and iodine. The factor loading matrix for the major nutrient patterns identified by PCA is illustrated in **Table 2**.

Characteristics of the participants across quartiles of four major nutrient patterns scores are indicated in Table 3. The mean age, FBG, body fat percentage, systolic, and diastolic blood pressure, marital status, and physical activity were not significantly different across quartile categories of four nutrient pattern scores. The participants with higher adherence to factor 1 nutrient pattern had a significant increase in WC, chronic disease, and drug use history. Also, it was found that higher adherence to factor 4 nutrient pattern, indicated a significant increase in BMI and visceral fat, and a significant decrease in pregnancy history. In addition, the participants who followed factor 3 nutrient pattern demonstrated the highest amount of the body muscle percentage. Moreover, the participants in the top quartile of factor 2 nutrient pattern, had the most history of chronic disease and using drugs compared to those in the lowest quartile.

Age- and energy-adjusted intakes of nutrients across quartile categories of nutrient pattern scores are illustrated in **Table 4**. The participants in the top quartile of factor 1 nutrient pattern, had the most intake of energy, carbohydrate, protein, fat, cholesterol, total fiber, SFA, and the lowest intake of EPA, DHA, and Iron. **Table 4** also indicates that an increase in adherence to factor 2 and factor 4 nutrient patterns had a considerable relationship with higher intakes of energy, carbohydrate, protein, fat, cholesterol, SFA, and increased intake of vitamin D in factor 3 nutrient pattern. In addition, moderate adherence to factor 3 nutrient patterns had a significant association with the lowest consumption of energy, fat, and cholesterol and the highest intake of EPA, DHA, and Iron.

Nutrient patterns and PCOS: Multivariable-adjusted OR and (95% CI for PCOS across quartile categories of nutrient patterns score are indicated in **Table 5**. After adjusting energy, individuals in the highest quartile of factor 1 and factor 4 nutrient patterns, tended to have higher odds of PCOS compared to those in the lowest quartile (OR = 4.85; 95% CI 1.12, 20.49; P_{trend} = 0.04) and (OR = 8.07; 95% CI 2.86, 22.47; P_{trend} = 0.04), respectively. This result remained significant after further adjustments for education, chronic disease history, socioeconomic status, diet history, marital status, pregnancy history, physical activity, body fat percentage, and visceral fat mass for factor 1 (OR= 7.50; 95% CI 2.78, 19.5; P_{trend} < 0.001), and factor 4 nutrient patterns (OR= 11.56; 95% CI 4.35, 30.88; P_{trend} < 0.001). Also, this association was observed after adjustment for energy intake, education, chronic disease history, socioeconomic, diet history, marital status, pregnancy history, physical activity, and WHR for factor 1 and factor 4 nutrient patterns (OR=7.42; 95% CI 2.86, 18.1; P_{trend} < 0.001) and (OR=11.32; 95% CI 4.3, 29.97; P_{trend} < 0.001), respectively. However, no significant result was observed between factor 2 nutrient pattern and the risk of PCOS before and after adjustments.

Tthe participants in the third quartile of factor 3 nutrient pattern, had a significant reduction in the risk of PCOS after adjustment for energy intake compared to those in the lowest quartile (OR=0.43; 95% CI 0.16, 0.82; P_{trend}= 0.001). Also, after adjustment for potential covariates in model 2, it was found that this result remained meaningful (OR=0.72; 95% CI 0.38, 0.92; P_{trend}=0.04). This association was observed after fully adjustment (OR=0.77; 95% CI 0.39, 0.98; P_{trend} = 0.04).

Table 1 General characteristics, energy, and physical activity of women with and without PCOS

Variables **Quantitative variables**	**Case** **Mean ± SD**	**Control** **Mean ± SD**	**P-value**[a]
Age (year)	28.95±7.16	30.45±7.17	0.83
Weight (kg)	70.07±12.95	70.11±13.01	0.72
Body mass index (kg/m^2)	27.10±4.88	26.63±4.87	0.87
Waist circumference (cm)	83.74±10.77	79.74±11.62	0.04
Hip circumference (cm)	82.74±10.77	79.74±11.62	0.44
Waist hip ratio	0.79±0.51	0.78±0.42	0.05
Fasting blood glucose (mg/dl)	101.26±15.50	89.37±11.42	0.01
Low density lipoprotein (mg/dl)	71.30±6.42	70.6±5.61	0.12
High density lipoprotein (mg/dl)	58.3±7.60	59.1±8.23	0.08
Fat mass (%)	40.75±6.81	42.29±6.83	0.32
Muscle mass (%)	24.39±3.14	23.67±2.52	0.35
Visceral Fat (%)	6.15±2.48	5.93±1.90	< 0.001
Socioeconomic status[b]	13.21±1.23	14.28±1.09	0.05
Energy intake (kcal)	2323.84±83.28	1882±566.84	< 0.001
Physical activity (MET-min/week)	987.00±201.22	1426.00±760.71	< 0.001
Qualitative variables	N (%)	N (%)	
Marital status			0.88
Single	35 (32.1)	40 (37.1)	
Married	69 (64.2)	65 (60.1)	
Separated	4 (3.7)	3 (2.8)	
Pregnancy history			0.68
No	45 (41.7)	49 (45.4)	
yes	63 (58.3)	59 (54.6)	
Chronic diseases history			1.00
No	61 (56.5)	62 (57.4)	
yes	47 (43.5)	46 (42.6)	
Drug use for PCOS[c]			1.00
No	61 (56.5)	62 (57.4)	
yes	47 (43.5)	46 (42.6)	
Education			0.05
Lower than diploma	14 (12.9)	16 (14.8)	
Diploma	37 (34.3)	26 (24.1)	
Above diploma	12 (11.1)	30 (27.8)	
Bachelor	35 (32.4)	29 (26.9)	
Master and above	10 (9.3)	7 (6.5)	

[a]: Independent t-test for quantitative variables and chi-square test for qualitative variables; [b]: socioeconomic status score was assessed based on education level, job, home status, and income level; [c]: Gastrointestinal, lipid-lowering drugs

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Table 2. The factor loading matrix for the major nutrient patterns identified by PCA.

Nutrients	Factor 1	Factor 2	Factor 3	Factor 4
Magnesium	0.795	0.350	0.306	0.274
Copper	0.783	0.459	-	0.281
Carbohydrate	0.759	-	0.241	0.316
Potassium	0.748	0.258	0.427	0.252
Selenium	0.712	0.247	0. 420	-
Phosphor	0.648	0.607	-	0.290
Vitamin C	0.647	-	0.456	-
Vitamin A	0.617	-	-	0.365
Manganese	0.489	-	-	0.489
Saturated fatty acids	0.344	0.711	-	0.536
Calcium	0.461	0.700	-	-
Cholesterol	-	0.681	-	-
Vitamin B (complex)	0.664	0.479	-	-
Vitamin D	-	0.670	0.342	-0.371
Zinc	0.450	0.662	0.217	0.423
Protein	0.468	0.567	0.348	0.216
Total fiber	-	0.479	0.712	-
Eicosapentaenoic acid (EPA)	-0.463	-	0.702	-
Docosahexaenoic acid (DHA)	-0.455	-	0.698	-
Chrome	0.437	-	0.527	-
Vitamin k	0.205	-	0.460	-0.302
Iron	-0.314	0.286	0.379	0.221
Monounsaturated fatty acids	0.267	0.415	-	0.789
Fat	0.374	0.378	-	0.786
Sodium	0.312	-	-	0.623
Vitamin E	0.209	-	-	0.601
Polyunsaturated fatty acids	-	0.235	0.313	0.524
Iodine	-	-	0.481	-0.238
Variance explained (%)	27.36	15.72	12.44	12.42

The cumulative percentage of variance explained by two nutrient patterns was 67.95%. Only items with correlation coefficients ≥ (0·20) were presented; PCA: Principal Component Analysis

Table 3. Characteristics by quartile (Q) categories of nutrient pattern scores in a sample of women with and without PCOS.

Variables	Quartiles				P-value[a]
	Q1	Q2	Q3	Q4	
Factor 1					
Age (year)	28.4 ± 0.9[b]	30.6 ± 0.9	29.7 ± 0.9	29.9 ± 1.0	0.48
Body mass index (kg/m²)	26.5 ± 0.6	26.1 ± 0.6	27.7 ± 0.6	27.0 ± 0.6	0.32
Waist circumference (cm)	79.0 ± 1.5	80.2 ± 1.8	84.4 ± 1.5	85.9 ± 1.8	0.02
Fasting blood glucose m/dl)	96.4 ± 2.1	94.5 ± 2.1	94.6 ± 1.6	95.5 ± 2.6	0.97
Body fat Percentage (%)	41.0 ± 0.9	41.2 ± 0.9	42.1 ± 0.8	40.8 ± 0.9	0.34
Body muscle Percentage (%)	23.1 ± 0.3	23.7 ± 0.3	24.0 ± 0.3	24.3 ± 0.4	0.16
Systolic blood pressure (mmHg)	12.3 ± 0.1	12.8 ± 0.1	12.0 ± 0.2	12.4 ± 0.2	0.80
Diastolic blood pressure (mmHg)	6.6 ± 0.2	6.7 ± 0.1	6.7 ± 0.3	7.0 ± 0.3	0.46
Visceral Fat (%)	5.8 ± 0.2	5.8 ± 0.1	6.4 ± 0.2	6.1 ± 0.2	0.56

Table 3. Characteristics by quartile (Q) categories of nutrient pattern scores in a sample of women with and without PCOS.

Variables	Quartiles				P-value[a]
	Q1	Q2	Q3	Q4	
Physical activity (MET- min /week)	1480 ± 858	1547 ±854	1331 ±649	1440 ± 722	0.72
Marital status (%)					
Single	40.7	33.3	35.2	38.9	0.85
Married	59.3	66.7	64.8	61.1	
Pregnancy history (%)					
Yes	59.3	57.4	50.0	59.3	0.74
No	40.7	42.6	50.0	40.7	
Chronic disease history (%)					
Yes	46.3	42.6	45.7	55.6	0.04
No	53.7	57.4	72.2	44.4	
Drug use (%)					
Yes	46.3	42.6	45.7	55.6	0.03
No	53.7	57.4	72.2	44.4	
Factor 2					
Age (year)	28.9 ± 0.9	29.7 ± 0.9	29.8 ± 0.9	30.3 ± 1.2	0.40
Body mass index (kg/m²)	26.5 ± 0.5	26.0 ± 0.5	26.8 ± 0.4	27.7 ± 0.4	0.57
Waist circumference (cm)	79.8 ± 1.2	80.1 ± 1.2	80.5 ± 1.3	83.5 ± 1.6	0.32
Fasting blood glucose m/dl)	96.4 ± 2.7	94.0 ± 1.8	95.2 ± 1.8	94.8 ± 2.6	0.87
Body fat Percentage (%)	41.1 ± 0.9	42.8 ± 0.7	41.3 ± 0.9	40.2 ± 0.8	0.67
Body muscle Percentage (%)	23.6 ± 0.3	23.7 ± 0.3	24.0 ± 0.3	24.6 ± 0.3	0.17
Systolic blood pressure (mmHg)	12.4 ± 0.1	12.0 ± 0.2	12.0 ± 0.1	12.5 ± 0.1	0.58
Diastolic blood pressure (mmHg)	7.0 ± 0.6	7.9 ± 0.5	7.6 ± 0.2	7.6 ± 0.6	0.11
Visceral Fat (%)	6.0 ± 0.2	5.8 ± 0.2	6.1 ± 0.2	6.2 ± 0.2	0.97
Physical activity (MET- min /week)	1547 ± 872	1438 ± 783	1518 ± 713	1334 ± 729	0.94
Marital status (%)					
Single	42.6	33.3	37.0	35.2	0.77
Married	57.4	66.7	63.0	64.8	
Pregnancy history (%)					
Yes	57.4	63.0	50.0	55.6	0.59
No	42.6	37.0	50.0	44.4	
Chronic disease history (%)					
Yes	51.9	33.3	31.5	55.6	0.02
No	48.1	66.7	68.5	444	
Drug use (%)					0.02
Yes	51.9	33.3	31.5	55.6	
No	48.1	66.7	68.5	444	
Factor 3					
Age (year)	28.3 ± 0.9	29.6 ± 0.9	30.5 ±	29.8 ± 1.0	0.45
Body mass index (kg/m²)	26.5 ± 0.6	26.1 ± 0.6	27.7 ± 0.6	26.7 ± 0.6	0.50
Waist circumference (cm)	79.0 ± 1.5	80.2 ± 1.8	83.4 ± 1.5	81.9 ± 1.8	0.19
Fasting blood glucose m/dl)	95.4 ± 2.1	93.5 ± 2.0	96.6 ± 1,6	95.5 ± 2.6	0.85
Body fat Percentage (%)	41.8 ± 0.9	41.2 ± 0.9	42.1 ± 0.8	40.8 ± 0.9	0.35
Body muscle Percentage (%)	23.1 ± 0.3	23.7 ± 0.3	24.0 ± 0.3	24.3 ± 0.4	0.04
Systolic blood pressure (mmHg)	12.3 ± 0.1	12.8 ± 0.1	12.0 ± 0.3	12.4 ± 0.2	0.71
Diastolic blood pressure (mmHg)	6.6 ± 0.2	6.7 ± 0.3	6.7 ± 0.2	7.0 ± 0.3	0.30
Visceral Fat (%)	6.5 ± 0.2	5.7 ± 0.2	5.6 ± 0.2	6.2 ± 0.2	0.17
Physical activity (MET- min /week)	1487 ± 650	1547 ± 902	1458 ± 753	1346 ± 763	0.74

Table 3. Characteristics by quartile (Q) categories of nutrient pattern scores in a sample of women with and without PCOS.

Variables	Quartiles				P-value[a]
	Q1	Q2	Q3	Q4	
Marital status (%)					
Single	35.2	44.4	35.2	33.3	0.62
Married	64.8	55.6	64.8	66.7	
Pregnancy history (%)					
Yes	57.4	64.8	50.0	53.7	0.45
No	42.6	35.2	50.0	46.3	
Chronic disease history (%)					
Yes	46.3	38.9	31.5	55.6	0.07
No	53.7	61.1	68.5	44.4	
Drug use (%)					0.07
Yes	46.3	38.9	31.5	55.6	
No	53.7	61.1	68.5	44.4	
Factor 4					
Age (year)	28.9 ± 0.9	30.7 ± 0.9	31.8 ± 0.9	28.3 ± 1.2	0.10
Body mass index (kg/m²)	25.5 ± 0.5	26.0 ± 0.5	27.5 ± 0.7	27.7 ± 0.7	0.04
Waist circumference (cm)	77.8 ± 1.2	81.1 ± 1.2	82.5 ± 1.3	83.5 ± 1.6	0.04
Fasting blood glucose m/dl)	94.4 ± 2.7	94.0 ± 1.8	95.2 ± 1.8	97.8 ± 2.6	0.68
Body fat Percentage (%)	40.1 ± 0.9	43.8 ± 0.7	41.0 ± 0.9	41.2 ± 0.8	0.24
Body muscle Percentage (%)	0.96	0.72	0.92	0.83	
Systolic blood pressure (mmHg)	23.6 ± 0.3	23.5 ± 0.3	24.0 ± 0.3	24.6 ± 0.3	0.83
Diastolic blood pressure (mmHg)	0.34	0.37	0.30	0.38	
Visceral Fat (%)	12.4 ± 0.1	12.0 ± 0.2	12.5 ± 0.1	12.8 ± 0.1	0.76
Physical activity (MET- min /week)	0.12	0.23	0.15	0.18	
Marital status (%)	7.0 ± 0.6	7.9 ± 0.5	7.6 ± 0.2	7.6 ± 0.6	0.23
Single	5.4 ± 0.2	6.5 ± 0.2	6.2 ± 0.2	6.9 ± 0.2	0.04
Married	1634 ± 103	1369 ± 100	1342 ± 98	1492 ± 105	0.19
Pregnancy history (%)					
Yes	48.1	27.8	31.5	40.7	0.12
No	51.9	72.2	68.5	59.3	
Chronic disease history (%)					
Yes	64.8	48.1	46.3	45.7	0.04
No	35.2	51.9	53.7	33.3	
Drug use (%)					
Yes	44.4	40.7	38.9	48.1	0.77
No	55.6	59.3	61.1	51.9	

Factor 1: loaded by high intake of vitamin B5, Biotin, Vitamin B1, Magnesium, fat, and sodium, and low in EPA, DHA, and iron; Factor 2: loaded by high intake of vitamin B12, saturated fatty acids, calcium, cholesterol, vitamin D, zinc, and fat; Factor 3: loaded by high intake of soluble and insoluble fiber, EPA, DHA, chrome, Potassium, vitamin C, polyunsaturated fatty acids, and iodine; Factor 4: loaded by high intake of monounsaturated fatty acids, fat, sodium, polyunsaturated fatty acids, saturated fatty acids, and manganese, and low in Vitamin D, vitamin K and iodine; [a]: ANOVA for continuous variables and χ2 test for categorical; [b:] mean ± SE

Table 4. Dietary intakes by quartile (Q) categories of nutrient pattern scores in a sample of women with and without PCOS.

Variables	Quartiles				P-value[a]
	Q1	Q2	Q3	Q4	
Factor 1					
Energy intake (kcal)	1399.1 ± 33.5[b]	1823.6 ± 41.5	2192.2 ± 52.5	2999.3 ± 89.5	<0.001
Carbohydrate (g)	198.1 ± 5.5	275.3 ± 8.5	323.6 ± 9.5	450.1 ± 14.3	<0.001
Protein (g)	58.1 ± 2.1	74.3 ± 2,4	85.7 ± 3.0	112.6 ± 4.5	<0.001
Fat (g)	44.1 ± 2.1	56.2 ± 2.6	68.4 ± 3.2	96.7 ± 4.5	<0.001
Cholesterol(mg)	188.3 ± 13.5	206.4 ± 12.1	243.4 ± 13.4	324.2 ± 15.5	<0.001
Total fiber (g)	0.36 ± 0.02	0.62 ± 0.02	0.86 ± 0.05	1.12 ± 0.08	<0.001
Ecosapantaenoic acid (mg)	0.009 ± 0.001	0.014 ± 0.001	0.025 ± 0.018	0.012 ± 0.007	0.001
Docosahexaenoeic acid (mg)	0.045 ± 0.004	0.036 ± 0.005	0.035 ± 0,001	0.034 ± 0.008	0.001
Saturated fatty acid (g)	14.1 ± 0.75	17.6 ± 0.79	20.8 ± 0.86	28.9 ± 0.99	<0.001
Vitamin D (µg)	0.94 ± 0.12	1.15 ± 0.16	1.16 ± 0.18	1.18 ± 0.21	0.06
Iron (mg)	26.1 ± 4.5	25.2 ± 4.2	23.3 ± 4.1	21.4 ± 3.6	<0.001
Poly unsaturated acid (g)	17.2 ± 0.75	19.2 ± 0.85	17.0 ± 0.73	16.6 ± 0.56	0.16
Factor 2					
Energy intake (kcal)	1499.1 ± 32.4	1823.6 ± 43.5	2122.2 ± 62.5	2989.3 ± 81.5	<0.001
Carbohydrate (g)	208.1 ± 5.5	266.3 ± 8.5	327.6 ± 9.5	440.1 ± 14.3	<0.001
Protein (g)	55.1 ± 2.1	74.3 ± 2.4	85.2 ± 4.0	115.6 ± 5.5	
Fat (g)	42.1 ± 2.2	56.2 ± 3.6	67.4 ± 3.8	99.7 ± 4.2	<0.001
Cholesterol(mg)	161.3 ± 12.5	226.4 ± 13.1	239.4 ± 14.4	334.2 ± 16.5	<0.001
Total fiber (g)	0.42 ± 0.01	0.56 ± 0.02	0.54 ± 0.03	0.55 ± 0.04	0.08
Ecosapantaenoic acid (mg)	0.009 ± 0.001	0.014 ± 0.001	0.015 ± 0.018	0.013 ± 0.007	0.12
Docosahexaenoeic acid (mg)	0.045 ± 0.004	0.036 ± 0.005	0.035 ± 0.001	0.034 ± 0.008	0.11
Saturated fatty acid (g)	12.1 ± 0.61	17.6 ± 0.72	20.8 ± 0.80	31.9 ± 1.20	<0.001
Vitamin D (µg)	0.84 ± 0.11	1.05 ± 0.14	1.14 ± 0.17	2.00 ± 0.23	<0.001
Iron (mg)	30.11 ± 4.50	35.23 ± 4.20	53.35 ± 4.10	51.45 ± 3.60	0.08
Poly unsaturated acid (g)	15.23 ± 0.35	21.22 ± 0.45	24.03 ± 0.53	24.63 ± 0.66	0.07
Factor 3					
Energy intake (kcal)	1539.1 ± 37.5	1723.1 ± 37.5	1713.6 ± 34.5	2151.2 ± 67.5	0.02
Carbohydrate (g)	214.1 ± 6.1	255.1 ± 6.3	325.3 ± 7.5	421.6 ± 8.5	<0.001
Protein (g)	61.1 ± 3.1	70.1 ± 2.1	84.3 ± 2.4	110.7 ± 3.0	<0.001
Fat (g)	48.1 ± 2.0	65.1 ± 2.1	56.2 ± 2.4	65.4 ± 3.2	<0.001
Cholesterol(mg)	197.3 ± 14.4	207.3 ± 14.5	188.4 ± 15.1	203.4 ± 13.4	<0.001
Total fiber (g)	0.347 ± 0.01	0.607 ± 0.02	0.823 ± 0.03	1.24 ± 0.07	<0.001
Ecosapantaenoic acid (mg)	0.001 ± 0.001	0.015 ± 0.001	0.028 ± 0.024	0.025 ± 0.021	0.001
Docosahexaenoeic acid (mg)	0.023 ± 0.001	0.039 ± 0.004	0.075 ± 0.05	0.061 ± 0.01	0.001
Saturated fatty acid (g)	15.1 ± 0.61	21.6 ± 0.72	21.8 ± 0.80	21.9 ± 1.20	0.12
Vitamin D (µg)	1.04 ± 0.11	1.08 ± 0.14	1.44 ± 0.17	1.80 ± 0.23	0.04
Iron (mg)	29.11 ± 4.5	28.23 ± 3.2	65.35 ± 12.1	48.45 ± 7.6	0.002
Poly unsaturated acid (g)	17.23 ± 1.35	19.22 ± 1.45	25.03 ± 2.53	34.63 ± 3.06	<0.001
Factor 4					
Energy intake (kcal)	1599.1 ± 37.5	1887.1 ± 37.5	2225.2 ± 59.3	2615.7 ± 114.2	<0.001
Carbohydrate (g)	240.1 ± 6.5	286.1 ± 6.5	335.8 ±8.4	382.6 ± 11.6	<0.001
Protein (g)	65.1 ± 3.1	74.1 ± 3.1	87.3 ± 3.6	104.5 ± 3.9	<0.001
Fat (g)	46.1 ± 2.0	55.1 ± 2.4	68.2 ± 2.6	94.4 ± 3.8	<0.001
Cholesterol(mg)	192.3 ± 14.4	206.3 ± 14.4	250.4 ± 15.2	303.4 ± 13.3	<0.001
Total fiber (g)	0.577 ± 0.01	0.677 ± 0.01	0.983 ± 0.03	9.861 ± 0.05	0.07

Table 4. Dietary intakes by quartile (Q) categories of nutrient pattern scores in a sample of women with and without PCOS.

Variables	Quartiles				P-value[a]
	Q1	Q2	Q3	Q4	
Ecosapantaenoic acid (mg)	0.017 ± 0.001	0.017 ± 0.001	0.016 ± 0.001	0.015 ± 0.017	0.96
Docosahexaenoeic acid (mg)	0.046 ± 0.001	0.044 ± 0.001	0.050 ± 0.001	0.045 ± 0.001	0.96
Saturated fatty acid (g)	14.1 ± 0.71	16.6 ± 0.78	21.8 ± 0.80	28.9 ± 1.30	<0.001
Vitamin D (µg)	1.24 ± 0.11	1.28 ± 0.14	1.40 ± 0.17	1.45 ± 0.23	0.59
Iron (mg)	40.11 ± 6.5	45.23 ± 9.2	33.35 ± 4.1	41.45 ± 9.6	0.90
Poly unsaturated acid (g)	17.23 ± 1.35	24.22 ± 2.45	20.03 ± 1.53	19.63 ± 2.06	0.001

Factor 1: loaded by high intake of vitamin B5, Biotin, Vitamin B1, Magnesium, fat, and sodium, and low in EPA, DHA, and iron; Factor 2: loaded by high intake of vitamin B12, saturated fatty acids, calcium, cholesterol, vitamin D, zinc, and fat; Factor 3: loaded by high intake of soluble and insoluble fiber, EPA, DHA, chrome, Potassium, vitamin C, polyunsaturated fatty acids, and iodine; Factor 4: loaded by high intake of monounsaturated fatty acids, fat, sodium, polyunsaturated fatty acids, saturated fatty acids, and manganese, and low in Vitamin D, vitamin K and iodine; [a]: ANOVA for continuous variables and $\chi 2$ test for categorical variables were used; [b]: mean ± SE

Table 5. Multivariate adjusted OR and 95% CI for PCOS among Quartile of nutrient patterns

	Q1	Q2	Q3	Q4	P_{trend}
Factor 1					
Model 1[a]	1	0.65 (0.27 –1.53)	1.21 (0.46–3.14)	4.85 (1.12-20.49)	0.04
Model 2[b]	1	0.64 (0.240 –1.66)	1.41 (0.50– .93)	4.68 (1.08–21.70)	0.04
Model 3[c]	1	0.73 (0.30– .77)	1.7 (0.78–4.01)	7.5 (2.78 –19.5)	<0.001
Model 4[d]	1	0.68 (0.28– .62)	1. 69 (0.74–3.80)	7.42 (2.86–18.1)	<0.001
Factor 2					
Model 1	1	0.67 (0.29-1.50)	0.95 (0.36-2.46)	2.41 (0.66 -9.47)	0.30
Model 2	1	0.54 (0.21-1.37)	0.97 (0.34-2.81)	1.99 (0.47-8.41)	0.36
Model 3	1	0.71(0.30-1.73)	1.63 (0.71-3.71)	1.86 (2.85-13. 88)	0.38
Model 4	1	0.67(0.280-1.59)	1.68 (0.71-3.03)	1.89 (2.13-13.17)	0.39
Factor 3					
Model 1	1	0.62 (0.29-1.30)	0.43 (0.16-0.82)	1.41 (0.46 -4.47)	0.001
Model 2	1	0.67 (0.28-1.57)	0.49 (0.19-0.87)	1.35 (0.48-4.71)	0.02
Model 3	1	0.82 (0.37-1.93)	0.72 (0.38- 0.92)	1.06 (1.85-11. 88)	0.04
Model 4	1	0.84 (0.37-1.07)	0.77 (0.39- 0.98)	1.5 (1.83- 9.97)	0.04
Factor 4					
Model 1	1	1.17 (0.51-2.85)	3.95 (1.65-9. 6)	8.07 (2.86-22.47)	<0.001
Model 2	1	1.01 (0.39-2.57)	3.22 (1.20-8.2)	7.76 (2.66-23.21)	<0.001
Model 3	1	1.11 (0.39-2.73)	4.06 (1.62–9.61)	11.56 (4.35 -30.88)	<0.001
Model 4	1	1.05 (0.42-2.6)	4.11 (1.7-9. 81)	11.32 (4. 3- 29.97)	<0.001

Factor 1: loaded by high intake of vitamin B5, Biotin, Vitamin B1, Magnesium, fat, and sodium, and low in EPA, DHA, and iron; Factor 2: loaded by high intake of vitamin B12, saturated fatty acids, calcium, cholesterol, vitamin D, zinc, and fat; Factor 3: loaded by high intake of soluble and insoluble fiber, EPA, DHA, chrome, Potassium, vitamin C, polyunsaturated fatty acids, and iodine; Factor 4: loaded by high intake of monounsaturated fatty acids, fat, sodium, polyunsaturated fatty acids, saturated fatty acids, and manganese, and low in Vitamin D, vitamin K and iodine;[a]: Adjusted for energy intake; [b]: Adjusted for energy intake, education, chronic disease history, socioeconomic, diet history, marital status, pregnancy history, physical activity, and body fat percentage; [c]: Adjusted for energy intake, education, chronic disease history, socioeconomic, diet history, marital status, pregnancy history, physical activity, body fat percentage, and visceral fat mass;[d]: Adjusted for energy intake, education, chronic disease history, socioeconomic, diet history, marital status, pregnancy history, physical activity, and WHR Q quartile of dietary pattern score.

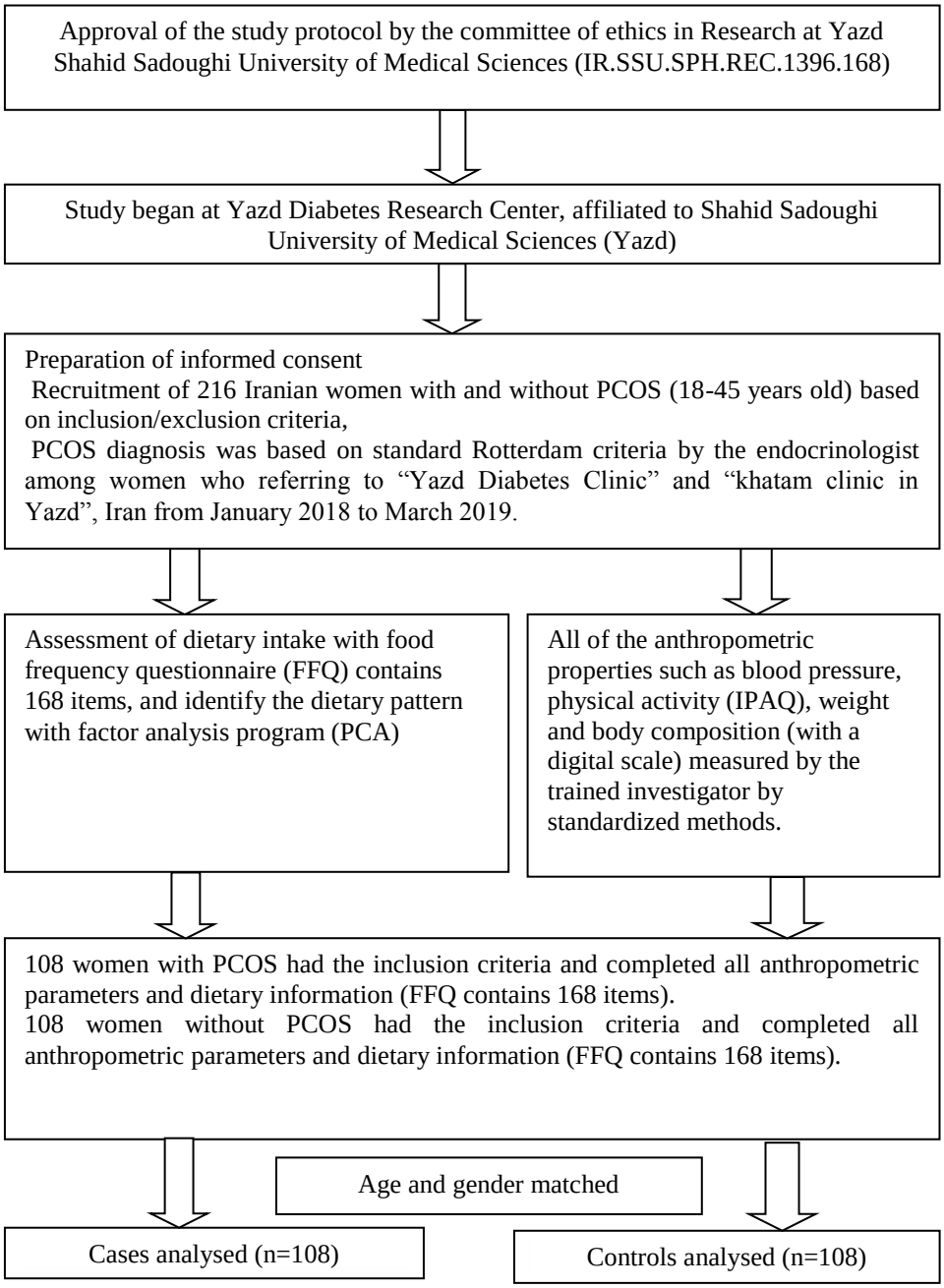

Figure 1. Flow chart of selection and enrollment of the study subjects (cases and controls) at the present study

Discussion

In this age and BMI matched case-control study, it was observed that nutrient patterns (factors 1 and 4) had an incremental effect on the odds of PCOS, while moderate adherence to the nutrient pattern (factor 3) had a reduction effect on the risk of PCOS. The number of studies that evaluated the association between major nutrient patterns and PCOS is very limited, and to the best of the authors' knowledge, this study is among the first investigations to evaluate the association between major nutrient patterns with odds of PCOS. Body composition was

also used as potential confounders between nutrient patterns and PCOS.

PCOS is highly prevalent worldwide, which can lead to hormonal, metabolic, and fertility disorders which results in decreased quality of life (Goodarzi *et al.*, 2011, Palomba *et al.*, 2015a). A significant increasing association was found between factor 1 nutrient pattern (which was rich in carbohydrate, potassium, vitamin B (complex), saturated fatty acids, fat, and low in EPA, DHA, and iron) and PCOS. These findings are in line with a study which indicated that a diet enriched in simple carbohydrates and SFA may reduce overall fertility (Bishop *et al.*, 2018). A pilot study also found that the intake of simple sugar was significantly higher in PCOS women compared to the control group. An observational study indicated that intake of potassium, folate, niacin, and iron was significantly more in the PCOS group compared to the control group (Moran *et al.*, 2013). On the other hand, some studies are not in line with the findings of the present study. For example, a study indicated a positive relationship between serum iron levels and PCOS (Rashidi *et al.*, 2017). Another study (Szczuko *et al.*, 2016) showed that women with PCOS had insufficient intake of potassium, folic acid, and vitamin B12, which is not consistent with the present study results. There are some possible mechanisms. Carbohydrates and saturated fats by increasing the prevalence of obesity, insulin resistance, and consequently hyperinsulinemia can play a pivotal role in hyperandrogenemia (Ding *et al.*, 2006, Gambineri *et al.*, 2002, Varlamov, 2017) and reduction of sex hormone-binding globulin (SHBG) (Pugeat *et al.*, 1991). This hyperandrogenemia may promote lipogenesis and inhibit lipolysis, which promotes the accumulation of visceral fat, and is associated with suppressed ovulation in PCOS (Nestler, 2000, Norman *et al.*, 2006, Rosenfield and Ehrmann, 2016). Another suggested mechanism is the low levels of EPA and DHA which have a protective role in insulin resistance (Mohammadi *et al.*, 2012, Sadeghi *et al.*, 2017).

It was also found that moderate adherence to factor 3 nutrient pattern, including total fiber, EPA, DHA, chrome, vitamin C, Vitamin D, potassium, magnesium, selenium, and PUFA, decreased the odds of PCOS. However, strong adherence to this dietary pattern did not indicate this protective effect on PCOS. It could be due to fact that factor 3 nutrient pattern was lacking some useful nutrients, such as vitamin B (complex), vitamin E, vitamin A, and calcium, which their beneficial effects on PCOS have been reported in previous studies (Izadi *et al.*, 2019, Kaya *et al.*, 2009, Shojaeian *et al.*, 2019). In line with the present study findings, some studies have indicated some useful effects of selenium and magnesium (Faghfoori *et al.*, 2017), chromium (Amr and Abdel-Rahim, 2015, Fazelian *et al.*, 2017), vitamin D (Panjeshahin *et al.*, 2019, Razavi *et al.*, 2016, Shojaeian *et al.*, 2019), consumption of fiber (Faghfoori *et al.*, 2017), and omega-3 (Mohammadi *et al.*, 2012, Sadeghi *et al.*, 2017) on the improvement of PCOS. A case-control study indicated that there was not any significant correlation between serum magnesium level and PCOS (Kanafchian *et al.*, 2020), which is not in line with the current study. An observational study indicated that the intake of potassium, magnesium and total fiber was significantly higher in PCOS women in comparison with healthy women, which is not consistent with the present stusy (Moran *et al.*, 2013). Some possible mechanisms, such as the effect of selenium and magnesium on the decrease of serum testosterone (Faghfoori *et al.*, 2017), and chromium on the increase of insulin sensitivity (Amr and Abdel-Rahim, 2015, Fazelian *et al.*, 2017) have been considered. Also, double bond unsaturated fatty acids, such as omega-3 (EPA and DHA) may increase (n-3/n-6) ratio that overcomes insulin resistance by preventing serine phosphorylation (Kalgaonkar *et al.*, 2011, Sadeghi *et al.*, 2017).

However, the current study indicated that there was a significant direct relationship between strong adherence to factor 4 nutrient pattern and the risk of PCOS. This nutrient pattern was high in fat, sodium, SFA, and low in vitamin D, vitamin k, and iodine. These findings are in line with a study indicating that women with PCOS had a higher mean consumption of total fat, SFA, and a lower intake of vitamin D(Szczuko *et al.*, 2016). A cohort study found that a western-style diet enriched in SFA reduced the overall fertility (Bishop *et al.*, 2018). On the other hand, this nutrient pattern was low in vitamin D and vitamin k which their useful effect on free testosterone, plasma TAC, serum triglycerides, and insulin metabolism in PCOS women have been reported before (Karamali *et al.*, 2017, Razavi *et al.*, 2016). The possible mechanisms are the same as factor 1 nutrient pattern. In addition, saturated fatty acids and sodium could increase serum level of insulin-like growth factor (IGF)-I, and production of ovarian theca-interstitial cells that might lead to PCOS (Chavarro *et al.*, 2008, Duleba *et al.*, 1998). SFAs may increase visceral fat and obesity which resulted in insulin resistance and hyperandrogenemia (Frayn, 2000, McCartney *et al.*, 2006, Nestler, 2000).

There were several strengths in this study. First of all, this study was one of the first studies that investigate the association between major nutrient patterns and odds of PCOS in a Middle Eastern country. Also, newly diagnosed PCOS women (incident) as a case group was considered to reduce the possibility of a conscious choice of a healthy diet by PCOS women. Furthermore, a wide range of confounders were checked, especially body composition. In addition, matching for age and BMI should be kept in mind. Also, the detail of FFQ specifically developed and validated for our population. To reduce self-reporting error, the FFQ was filled out by an expert dietitian who was blinded and unaware of which participants would be in the case or control groups. Furthermore, important covariates, such as waist-to-hip ratio (WHR), body fat percentage, and visceral fat mass as potential confounders were adjusted, which could have an effective relation on PCOS.

However, this study had some limitations. One of them was the risk of recall bias that may occur during the use of semi-quantitative FFQ. Another limitation was using factor analysis to identify nutrient patterns, since this method included some individual decisions, such as the selection of nutrient groups, the number of factors extracted, and the method of rotation and nomination of dietary patterns.

The present study indicated some significant relationships between major nutrient patterns and PCOS. The current findings recommend women population increase consumption of the nutrient pattern, including high intakes of total fiber, EPA, DHA, chrome, vitamin C and D, potassium, iron, and PUFA, to protect them against PCOS. However, due to the low ability of case-control studies in evaluating the causality effect, further prospective studies are required to confirm or refute the results of the current study.

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Authors' contribution

Hosseinzadeh M: conceptualization, supervision, writing - review and editing, project administration. Panjeshahin A: First author, writing the original draft, investigation, methodology, software, formal analysis, data curation. Ghadiri-Anari A: Resources. Salehi-Abargouei A: Review and editing. Rasouli A: Review and editing.

Conflicts of interest

The authors declare that there is no conflict of interest.

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