BMC Nutrition

RESEARCH Open Access

# The association between Lifelines Diet Score (LLDS) and Polycystic Ovary Syndrome (PCOS) in Iranian women: a case-control study

Mina Darand[1], Vahid Arabi[2,3], Moloud Ghorbani[4], Zahra Salimi[5] and Mahdieh Hosseinzadeh[2,3*]

## Abstract

**Background** Although adherence to a healthy dietary pattern is one of the primary recommendations for the prevention of polycystic ovary syndrome (PCOS), there is still no conclusive evidence of which specific dietary pattern is best. The Lifelines diet score (LLDS) is a new, evidence-based scoring system to determine diet quality, and its association with PCOS has not been investigated. The present study aimed to assess the association between LLDS and PCOS in Iranian women.

**Materials and methods** This frequency-matched case-control study was carried out on 108 women with PCOS and 108 women without PCOS as a control group in Yazd, Iran. Healthy controls were matched to PCOS women based on age and BMI. The validated 178-item food frequency questionnaire was used to assess the usual dietary intake. Logistic regression was used to estimate the association between LLDS and PCOS.

**Results** The findings of the present study showed women in the highest tertile of LLDS compared with the participants in the lowest tertile had 90% lower odds of PCOS (Odds Ratio (OR): 0.10; 95% Confidence Interval (CI): 0.04 to 0.21, p for trend: <0.001). This association remained significant after adjustment for energy intake, marital status, pregnancy history, WC, chronic disease history, physical activity, and BMI (Odds Ratio (OR): 0.11; 95% (CI):0.05 to 0.27, p for trend: <0.001).

**Conclusion** Although the present study found a significant protective association between adherence to LLDS and PCOS, more mechanism-based studies are needed to confirm these findings in the future.

**Keywords** Lifelines diet score, PCOS, Polycystic ovary syndrome

*Correspondence:
Mahdieh Hosseinzadeh
hoseinzade.mahdie@gmail.com
[1]Prevention of Cardiovascular Disease Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Research Center for Food Hygiene and Safety, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[3]Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[4]Department of Community Nutrition, Faculty of Nutrition and Food Sciences, Tabriz University of Medical Sciences, Tabriz, Iran
[5]Student Research Committee, Department of Clinical Nutrition and Dietetics, Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

## Introduction

Polycystic ovary syndrome is considered one of the major health problems in the world [1] and is a common and complicated endocrinopathy with 6–20% prevalence among women in the childbearing period [2, 3]. This syndrome is marked by various phenotypes and is recognized when at least two of the three Rotterdam criteria exist: first, clinical hyperandrogenism and/or high levels of circulating androgens; second, the existence of ovarian cysts diagnosed by ultrasound examination; and third, oligo-amenorrhea with oligo-anovulation [4]. PCOS also has detrimental outcomes and is associated with metabolic disorders and type 2 diabetes (T2D), cardiovascular and cerebrovascular traumas, obstetric comorbidities, infertility, mood disturbances, and endometrial and ovarian cancer [5]. Although the pathogenesis of PCOS is complex and not exactly clear, studies refer to the role of genetic or modifiable agents such as environmental and lifestyle factors. However, unfavorable lifestyle especially unhealthy dietary patterns, causes insulin resistance and obesity as etiological factors in this syndrome [6, 7]. Lifestyle amendments particularly dietary intake and physical activity have an important role in the clinical management of PCOS to improve its adverse consequences in women [8]. Previous research was mainly focused on the association between single diet components and PCOS [9, 10]. Dietary patterns show the variety of daily food intakes compared with a single food item. Therefore, dietary patterns are considered a good indicator of the type of diet that people usually consume [11]. Several studies demonstrated that higher adherence to healthy dietary patterns was inversely associated with PCOS [12–14]. A systematic review showed that the diet, which appears to improve the clinical and laboratory markers of this syndrome, includes: fruits and vegetables (non-starchy and with low glycemic index), low-fat dairy products (in small quantities), lean red meat and poultry (in small amounts), fish (rich in ω-3 fatty acids), whole grain, legumes, fatty acids and alcohol (in moderation) [15].

Lifeline Diet Score (LLDS) is a novel food-based score according to the Dutch Dietary Guidelines used to unveil the association between diseases and diets [16]. Results of a 7.6-year prospective analysis of the Dutch Lifelines cohort showed that higher scores are associated with a lower risk of type 2 diabetes and all-cause mortality [17, 18]. It has been reported that a diet low in total fat and saturated fats and rich in fruits and vegetables can decline inflammatory indicators [19] and result in reduced risk of insulin resistance, cardiovascular disease, and cancers [20, 21]. Also, two surveys illustrated that higher LLDS respectively decreased the odds of metabolically unhealthy and breast cancer in women [22, 23].

Due to the emergence of the LLDS as a novel evidence-based scoring system for assessing diet quality and the lack of investigation of its relationship with PCOS in the population of Iranian women, it was decided to investigate the association between LLDS and PCOS.

## Materials and methods

### Study population

This frequency-matched case-control was conducted on 216 women (108 new cases diagnosed with PCOS and women without PCOS) who attended the Yazd Diabetes Clinic and Khatam Clinic in Yazd from January 2018 to March 2019. Women with PCOS were diagnosed based on Rotterdam criteria and the presence of at least two of the three following criteria: menstrual irregularities, clinical or biochemical signs of hyperandrogenism, and polycystic ovaries (≥12 follicles measuring 2–9 mm in diameter and/or an ovarian volume>10 mL in at least one ovary) [4]. The inclusion criteria of the case group were as follows: women of reproductive age (18 to 45 y) diagnosed as new PCOS cases; women with no history of diseases such as hypothyroidism, hyperprolactinemia, congenital adrenal hyperplasia, Cushing syndrome, or food allergies; women without type 1 diabetes; women with no history of using drugs such as medications that could change the density of androgens or hormonal drugs; women who did not drink alcohol and were not smokers; and women who did not have a specific diet during the last year. The control group included women without PCOS (lacking Rotterdam diagnostic criteria) who had been referred to other departments of the same clinic such as orthopedics, dentistry, or optometry. Healthy controls were matched to PCOS women based on age and BMI. Other inclusion criteria were almost identical for the case and control groups. The participants' recruitment procedures are represented in Fig. 1.

### Sample size calculation

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

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

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

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

Where $P = \frac{P_1+P_2}{2}$, $Q = 1 - P$, $Q_1 = 1 - P_1$, $Q_2 = 1 - P_2$

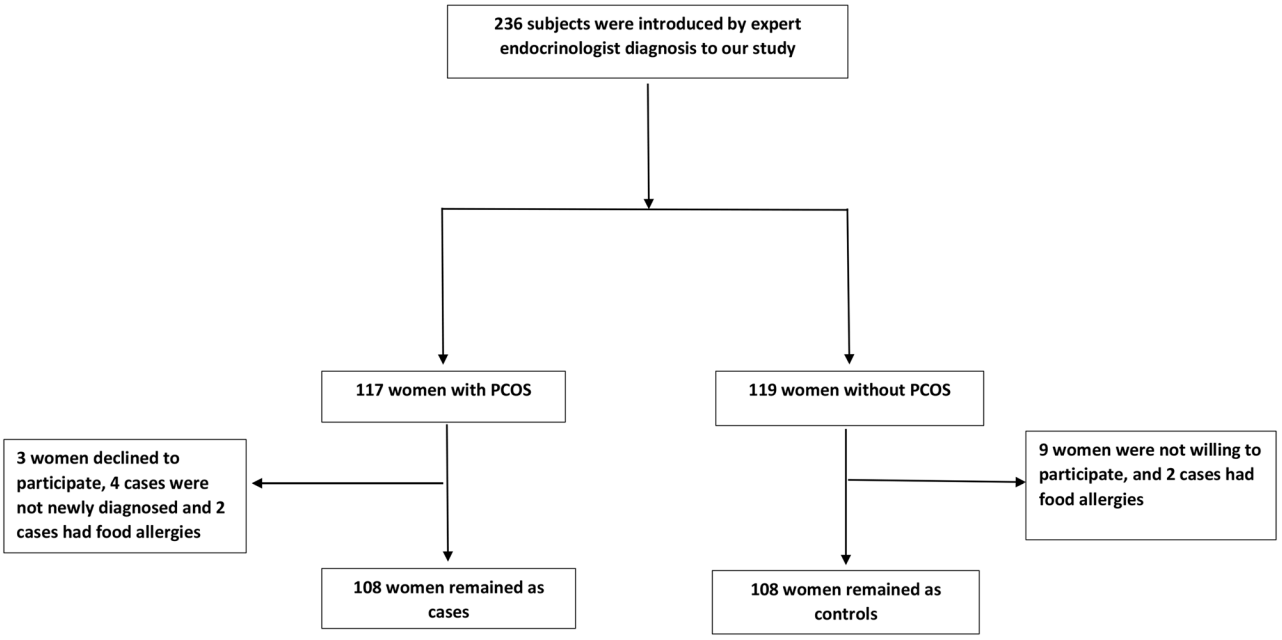


**Fig. 1** The participants' recruitment procedures are represented in Fig. 1

### Dietary intake assessment

After the recruitment, participants' dietary intake over the past year was evaluated using a validated 178-item food frequency questionnaire (FFQ) with 551 questions. This questionnaire was validated in previous studies [24]. Portion sizes and frequency of food items were questioned by a blinded trained dietitian with face-to-face interviews. The frequency response for food intake included 10 categories as follows: "never or <1 time/month" to "10 times or more/day". Then, the frequency was converted into daily intake and converted to grams based on household measures. Eventually, the actual food consumption (g/d) was transferred to Nutritionist IV to calculate the total energy and nutrient intake.

### Lifelines diet score

The LLDS, a tool for ranking people in the relative quality of their diet, was calculated based on the Vinke et al. method [16]. According to the LLDS guidelines, food groups were classified as having positive, neutral, negative, or unknown health effects. Foods in the nine groups with positive health effects include legumes and nuts, whole grain products, fruits, vegetables, fish, unsweetened dairy, coffee and tea, soft margarine, and oils. Butter and hard margarine, sugar-sweetened beverages, and red and processed meat are three groups that have a negative impact on health. Each participant's food consumption was measured in grams per 1000 kilocalories (kcal) and then divided into quintiles from 1 to 5 points. Patients in the highest quintile of each positive food group's intake were given 5 points and those assigned to the lowest quintile were given 1 point. For food groups with negative effects on health, point 1 represents the maximum, and point 5 represents the minimum dietary intake. The scores summation for the consumption of 12 food groups consisting of LLDS ranged from 12 to 60 points [16].

### Covariate measurements

All the anthropometric measurements were done in a fasting state using standard protocols by a trained investigator. Subsequently, BMI was calculated by dividing the person's weight (kg) by the square of height (m2). Waist circumference (cm) was measured using a tape measure with an accuracy of 0.5 cm at the midpoint between the lower rib and iliac crest at the end of a normal exhalation in a standing position. Physical activity data was evaluated using an International Physical Activity Questionnaire-Short Form (IPAQ-SH) [25] and expressed as metabolic equivalent in min per week (MET-min/wk).

### Assessment of other covariates

Needed information including demographic data, age, chronic diseases (Diabetes and hypertension), marital status and pregnancy history was acquired by using validated self-administered questionnaires.

### Statistical analysis

Quantitative and qualitative participants' characteristics were compared by an independent t-test and chi-square test, respectively. The ANOVA test was used to compare the dietary intakes in tertiles of LLDS. Logistic regression was used to evaluate the association between the Lifelines diet and PCOS in adjusted and crude models. The

**Table 1** General characteristics of women with and without PCOS

| Variables | Case ($n=108$) | Control ($n=108$) | *P* value* |
|---|---|---|---|
| **Age (y)** | 28.95 ± 7.16 | 30.45 ± 7.17 | 0.126 |
| **BMI (kg/m2)** | 27.10 ± 4.88 | 26.63 ± 4.87 | 0.482 |
| **WC (cm)** | 82.74 ± 10.77 | 79.74 ± 11.62 | 0.051 |
| **PA (MET-min/wk)** | 1426.24 ± 760.70 | 1493.55 ± 793.42 | 0.525 |
| **Marital status (n (%))** | 39(36.1) | 41(38) | 0.778 |
| Single | 69(63.9) | 67(62) | |
| Married | | | |
| **Pregnancy history (n (%))** | 45(41.7) | 49(45.4) | 0.583 |
| No | 63(58.3) | 59(58.3) | |
| Yes | | | |
| **Chronic disease history (n (%))** | 61(56.5) | 62(57.4) | 0.891 |
| Yes | 47(43.5) | 46(42.6) | |
| No | | | |
| **LLDS (mean ± SD)** | 33.21 ± 5.94 | 39.10 ± 6.36 | < 0.001 |

BMI: body mass index; MET: metabolic equivalent; PA: physical activity; PCOS: polycystic ovary syndrome; WC: waist circumference, SES: socioeconomic status

For quantitative variables mean ± SD; and for qualitative variables frequency (%) were used

*Independent t-test for quantitative variables and $x^2$ test for categorical variables conducted

† Anti-diabetic and anti-hypertensive drugs

model I was adjusted for energy intake. Further adjustments were for marital status, pregnancy history, WC, disease history, and physical activity. The BMI was additionally adjusted in model III. P-values < 0.05 were considered statistically significant. Analyze the data used by the Statistical Package for Social Sciences (SPSS) (version 26.0, SPSS Inc., Chicago, Illinois, USA).

## Results

### General characteristics of the study population

General characteristics and physical activity of women with and without PCOS are presented in Table 1. As shown in this table, no statistically significant differences were detected in age, BMI, physical activity, marital status, pregnancy history, and disease history between the case and control group ($P>0.05$), while the WC in the case group was marginally larger than the control group ($P=0.051$). Also, the mean LLDS in the control group (39.10 ± 6.36) was significantly higher than the case group (33.21 ± 5.94) ($P<0.001$).

Table 2 shows the characteristics of the study population across tertiles of the Lifelines Diet Score. After LLDS score categorization into three groups (tertiles), no statistically significant differences were observed in age, BMI, WC, physical activity, marital status, pregnancy history, and chronic disease history across tertiles of the LLD scores ($P>0.05$), while the prevalence of PCOS differed significantly across tertiles of the LLD scores ($P<0.001$).

### Dietary intakes of participants

Table 3 shows the study patients' energy and dietary intakes based on tertiles of LLD scores. The individuals in the highest LLDS tertile had significantly greater intakes of carbohydrates, calcium, magnesium, and folate ($p<0.001$), but significantly lower consumption of energy, fat, saturated fatty acid, and monounsaturated fatty acid ($p<0.001$). Intake of protein, polyunsaturated fatty acid, vitamin B6, and vitamin B12 was not significantly different between tertiles of LLDS). Based on food group intake, participants with a higher score for the LLDS had a significantly higher intake of vegetables, whole grain products, legumes and nuts, fish, oils and soft margarine, coffee and unsweetened dairy; whereas, they had a lower

**Table 2** Characteristics of the study participants across tertiles of LLDS *

| Variable | Tertiles of LLDS | | | *P*-value** |
|---|---|---|---|---|
| | T1 (≤ 20) | T2 (33–38) | T3 (39 ≤) | |
| **Age (year)** | 29.01 ± 7.38 | 30.01 ± 7.16 | 30.05 ± 7.09 | 0.621 |
| **BMI (kg/m2)** | 26.63 ± 5.42 | 27.51 ± 4.97 | 26.47 ± 4.17 | 0.384 |
| **WC (cm)** | 81.18 ± 12.99 | 82.40 ± 11.33 | 80.20 ± 10.73 | 0.501 |
| **PA (*MET-min*/week)** | 1518.69 + 828.90 | 1423.80 + 726.55 | 1439.19 + 778.04 | 0.729 |
| **Marital status (n (%))** | 28(40) | 27(38) | 25(33.3) | 0.332 |
| Singel | 42(60) | 44(62) | 50(66.7) | |
| Married | | | | |
| **Pregnancy history (n (%))** | 25(35.7) | 30(42.3) | 39(52) | 0.137 |
| No | 45(64.3) | 41(57.7) | 36(48) | |
| Yes | | | | |
| **Chronic disease history (n (%))†** | 31(44.3) | 39(54.9) | 23(30.7) | 0.012 |
| Yes | 39(55.7) | 32(45.1) | 52(69.3) | |
| No | | | | |
| **PCOS (n (%))** | | | | 0 < 0.001 |
| No | 17(24.3) | 34(47.9) | 57(76) | |
| Yes | 53(75.7) | 37(52.1) | 18(24) | |

**Table 3** Dietary intakes of study participants based on tertiles of LLDS

| Variable | Tertiles of LLDS | | | *P*-value** |
|---|---|---|---|---|
| | T1 (≤ 20) | T2 (33–38) | T3 (39 ≤) | |
| Energy intake (kcal)* | 2372.14 ± 721.79 | 2106.41 ± 781.16 | 1849.57 ± 585.41 | < 0.001 |
| Carbohydrate (% of total daily energy) | 55.62 ± 0.07 | 58.97 ± 0.06 | 62.32 ± 0.05 | < 0.001 |
| Protein (% of total daily energy) | 15.78 ± 0.03 | 15.44 ± 0.02 | 16.61 ± 0.02 | 0.054 |
| Fat (% of total daily energy) | 31.86 ± 0.05 | 28.27 ± 0.06 | 24.66 ± 0.05 | < 0.001 |
| Cholesterol (mg/100Kcal) | 115.56 ± 44.62 | 110.19 ± 49.75 | 115.10 ± 54.01 | 0.175 |
| SFA (gr/1000Kcal) | 11.05 ± 2.52 | 9.66 ± 2.56 | 8.24 ± 2.37 | < 0.001 |
| MUFA (gr/1000Kcal) | 11.11 ± 2.54 | 9.44 ± 2.35 | 7.80 ± 1.66 | < 0.001 |
| PUFA (gr/1000Kcal) | 9.75 ± 5.78 | 11.27 ± 7.90 | 12.52 ± 7.47 | 0.066 |
| Calcium (mg/1000Kcal) | 327.80 ± 96.74 | 398.08 ± 117.99 | 418.93 ± 100.85 | < 0.001 |
| Magnesium (mg/1000Kcal) | 115.67 ± 16.54 | 128.41 ± 20.38 | 137.85 ± 21.18 | < 0.001 |
| Vitamin B6 (mg/1000Kcal) | 0.80 ± 0.25 | 0.83 ± 0.25 | 0.89 ± 0.28 | 0.122 |
| Folate (µg/1000Kcal) | 122.48 ± 26.51 | 139.77 ± 36.11 | 158.53 ± 37.70 | < 0.001 |
| B12 (µg/1000Kcal) | 1.91 ± 0.85 | 1.73 ± 0.68 | 1.82 ± 0.59 | 0.319 |
| **Food groups** | | | | |
| Vegetables (gr/1000Kcal) | 72.42 ± 48.97 | 107.09 ± 59.49 | 168.08 ± 74.17 | < 0.001 |
| Fruits (gr/1000Kcal) | 308.03 ± 170.68 | 330.12 ± 182.67 | 366.20 ± 145.69 | 0.107 |
| Whole grain products (gram) | 7.57 ± 11.44 | 24.80 ± 34.34 | 52.46 ± 42.13 | < 0.001 |
| Legumes and nuts (gr/1000Kcal) | 17.03 ± 7.90 | 22.21 ± 12.01 | 28.84 ± 14.41 | < 0.001 |
| Fish (gram) | 3.36 ± 3.66 | 4.10 ± 3.53 | 6.67 ± 4.75 | < 0.001 |
| Oils and soft margarines (gram) | 3.01 ± 2.81 | 4.27 ± 3.29 | 5.94 ± 2.99 | < 0.001 |
| Unsweetened dairy (gram) | 85.30 ± 74.49 | 124.74 ± 102.09 | 135.16 ± 77.47 | 0.001 |
| Coffee (gram) | 3.90 ± 5.25 | 5.70 ± 16.77 | 8.34 ± 14.84 | < 0.001 |
| Tea (gram) | 146.20 ± 159.32 | 211.56 ± 306.23 | 179.79 ± 305.63 | 0.351 |
| Red and processed meat (gram) | 37.90 ± 19.26 | 24.97 ± 17.16 | 17.99 ± 15.25 | < 0.001 |
| Butter and hard margarines | 5.57 ± 5.79 | 3.18 ± 4.39 | 0.89 ± 1.45 | < 0.001 |
| Sugar sweetened beverages(gram) | 52.59 ± 56.07 | 24.55 ± 38.08 | 15.25 ± 35.51 | 0.001 |

MUFA, Monounsaturated Fatty Acid; PUFA, Ponounsaturated Fatty Acid; SFA, Saturated Fatty Acid; LLDS, lifelines diet score; PCOS, Polycystic ovary syndrome

* Data reported on mean ± standard deviation (SD)

** Obtained from one way Anova

Statistically significant difference (P-value < 0.05)

intake of red and processed meat, butter and hard margarine, and sugar-sweetened beverages ($p < 0.001$).

### Association between adherence to Lifelines diet and odds of PCOS

Crude and multivariate-adjusted odds ratios for occurrence of the PCOS across tertiles of LLDS in 108 cases are shown in Table 4. PCOS women in the highest tertile of LLDS compared with the participants in the lowest tertile had 90% lower odds of PCOS (Odds Ratio (OR): 0.10; 95% Confidence Interval: 0.04 to 0.21, p for trend: <0.001). This association remained significant after adjustment for energy intake, marital status, pregnancy history, WC, drug history, disease history, physical activity and BMI (Odds Ratio (OR): 0.11; 95% [14]:0.05 to 0.27, p for trend: <0.001).

## Discussion

To our knowledge, this study is the first to investigate the association between LLDS and PCOS among Iranian women. Our results illustrated that women in the highest tertile of LLDS had 90% lower odds of PCOS than those in the lowest tertile. As the LLD score increased, the average intake of positive food groups, including vegetables, whole grain products, legumes and nuts, oils and soft margarine, fish, coffee, and unsweetened dairy, significantly increased, although consumption of negative food groups, such as red and processed meat, butter and hard margarine, and sugar-sweetened beverages significantly decreased. Previous studies showed that adherence to a diet with a high LLDS decreased the odds of breast cancer and metabolically unhealthy in women [22, 23]. In addition, a higher score reduced the risk of type 2 diabetes and all-cause mortality in the Dutch Lifeline cohort [17, 18]. However, some studies have found no association between higher adherence to LLDS and novel anthropometric indices affecting polycystic ovary

**Table 4** Odds ratio and 95% confidence interval for occurrence of the PCOS across tertiles of LLDS in 108 cases

| PCOS | Tertiles of LLDS diet | | | *P*-value* | *P* trend |
|---|---|---|---|---|---|
| | T1 (≤ 20) | T2 (33–38) | T3 (39 ≤) | | |
| No. of cases | 17 | 34 | 57 | | |
| Crude | 1.00 | 0.34 (0.17_71) | 0.10 (0.04_0.21) | < 0.001 | < 0.001 |
| Model1 | 1.00 | 0.40 (0.19_0.83) | 0.13 (0.05_0.28) | < 0.001 | < 0.001 |
| Model2 | 1.00 | 0.39 (0.18–0.84) | 0.12 (0.05–0.27) | < 0.001 | < 0.001 |
| Model3 | 1.00 | 0.39 (0.18–0.85) | 0.11 (0.05–0.27) | < 0.001 | < 0.001 |

LLDS: lifelines diet score; PCOS, polycystic ovary syndrome

*Third tertile compared to first tertile

Model 1: adjusted for energy intake

Model 2: additionally, adjusted for marital status, pregnancy history, WC, chronic disease history (Diabetes and hypertension) and physical activity

Model 3: additionally, adjusted for BMI

syndrome such as A Body Shape Index, Body Roundness Index, and Body Adiposity Index [26–28].

In line with our results, some studies have shown that higher adherence to healthy dietary patterns is significantly inversely associated with PCOS and its related conditions [15]. Results from a study carried out on PCOS women with overweight and obesity indicated that consumption of a diet rich in whole grains, vegetables, fruits, and low-fat dairy and low in refined grains, sweets, cholesterol, and saturated fats, led to a significant reduction in serum levels of insulin and hs-CRP, HOMA-IR values, waist and hip circumference [29]. A cross-sectional/case-control study by Barrea et al. reported that women with PCOS had higher levels of testosterone, fasting insulin and glucose, and HOMA-IR than the control group. They found that women with PCOS had a lower intake of legumes, nuts, fish/seafood, and extra-virgin olive oil than the control group. Furthermore, women with PCOS consumed lesser amounts of fiber, complex carbohydrates, n-3 polyunsaturated fatty acids (PUFA), monounsaturated fatty acids (MUFA), and higher amounts of total fat, saturated fatty acids, simple carbohydrates, PUFA, and n-6 PUFA compared to the control group [14]. A cross-sectional study conducted in 2020 showed that diets rich in favorable agents, including fiber, vitamins, minerals, and other antioxidant ingredients, resulted in decreased glycemic disorders, insulin resistance, obesity, and hyperandrogenism and additionally led to satiety in women [30]. In a trial that was conducted on 60 women with PCOS, a higher intake of whole grains, vegetables, fruits, and low-fat dairy products, as well as a lower intake of refined grains, sweets, saturated fats, and cholesterol, led to a significant decrease in weight, body mass index (BMI), fat mass, and serum androstenedione, and a significant increase in sex hormone-binding globulin and antioxidant status [31].

Several mechanisms may explain the association between dietary intake and PCOS. A diet rich in fruits, vegetables, and nuts provides a considerable portion of the human potassium intake and reduces the sodium-to-potassium ratio. Based on previous evidence lower sodium-to-potassium ratios result in a lower risk of PCOS [32, 33]. However, unhealthy dietary patterns can result in chronic low-grade inflammation, either directly or indirectly [34, 35]. It has been suggested that inflammation and oxidative stress caused by nutrients can lead to metabolic disruption and ovarian dysfunction. For instance, glucose and saturated fats increase the number of circulating mononuclear cells, causing the activation of nuclear factor kappa B, subsequent induction of inflammation, and insulin resistance in PCOS [36, 37]. In addition to their direct outcomes, unhealthy dietary patterns can cause inflammation through the indirect effects of obesity; secretion of inflammatory cytokines occurs by the accumulation of dysfunctional adipocytes in white adipose tissue, and the infiltration of immune cells leads to inflammation [38]. Additionally, insulin resistance and other hormonal disturbances (including increased ghrelin levels) in women with PCOS lead to increased caloric intake, resulting in obesity and exacerbation of PCOS [39].

The Lifeline diet is rich in antioxidants contained in fruits, vegetables, and whole grains. In addition, this diet is a valuable source of dietary magnesium, which elevates the antioxidant capacity of the serum and tissues [40], reduces the activity of antioxidative enzymes, eliminates oxygen radicals [41], and decreases insulin resistance [42].

One of the strengths of this study was the use of a valid FFQ in the Iranian population. In addition, this is the first study to investigate the association between LLDS and PCOS among Iranian women, and results were adjusted for energy intake, marital status, pregnancy history, WC, drug history, and physical activity as confounder factors; however, there are limitations as well. First, due to the cross-sectional nature of this study, a causal relationship cannot be inferred. Second, recall biases are possible because of the retrospective and memory-dependent nature of FFQ. Third, a measurement bias is inevitable in any dietary assessment. Furthermore, despite controlling

for confounders, the effects of residual confounders could not be ruled out. Thus, a prospective study design with a larger sample size and longer duration is required to assess this relationship.

## Conclusion

Our results disclosed a significant protective association between adherence to LLDS and PCOS, more mechanism-based studies are needed to confirm these findings in the future.

#### Abbreviations

| | |
|---|---|
| BMI | Body Mass Index |
| CI | Confidence Interval |
| FFQ | quantitative food-frequency questionnaire |
| HC | Hip circumstance |
| HOMA-IR | Homeostatic Model Assessment for Insulin Resistance |
| IPAQ | International Physical Activity Questionnaire |
| LLDS | Lifelines diet score |
| MET | Metabolic Equivalent |
| MUFA | Monounsaturated Fatty Acid |
| OR | Odds Ratio |
| PCOS | Polycystic ovary syndrome |
| PUFA | Polyunsaturated Fatty Acid |
| SD | Standard Deviation |
| SES | socioeconomic status |
| SFA | Saturated Fatty Acid |
| WC | Waist Circumference |

#### Acknowledgements

Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

#### Author contributions

M.H: supervision, study concept; M.D: design analysis of data and drafting the manuscript; V.A, M.Gh and Z.S drafting the manuscript.

#### Funding

This article has no funding.

#### Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

#### Ethics approval and consent to participate

The survey was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Informed consent was taken from participants. This study was conducted in accordance with the Declaration of Helsinki. All methods were performed in accordance with the relevant guidelines and regulations.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare no competing interests.

Received: 9 May 2024 / Accepted: 12 September 2024
Published online: 10 October 2024

#### References

1. Bykowska-Derda A, Czlapka-Matyasik M, Kaluzna M, Ruchala M, Ziemnicka K. Diet quality scores in relation to fatness and nutritional knowledge in women with polycystic ovary syndrome: case–control study. Public Health Nutr. 2021;24(11):3389–98.
2. Ganie MA, Rashid A, Sahu D, Nisar S, Wani IA, Khan J. Prevalence of polycystic ovary syndrome (PCOS) among reproductive age women from Kashmir valley: a cross-sectional study. Int J Gynecol Obstet. 2020;149(2):231–6.
3. Ricardo A, Enrico C, ZiJiang C, Andrea D, Joop L. Polycystic ovary syndrome. Nat Rev Dis Primers. 2016;2:16057.
4. Group REASPCW. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19(1):41–7.
5. Azziz R, Carmina E, Chen Z, Dunaif A, Laven JS, Legro RS, et al. Polycystic ovary syndrome. Nat Reviews Disease Primers. 2016;2(1):1–18.
6. Witchel SF, Oberfield SE, Peña AS. Polycystic ovary syndrome: pathophysiology, presentation, and treatment with emphasis on adolescent girls. J Endocr Soc. 2019;3(8):1545–73.
7. Rostamtabar M, Esmaeilzadeh S, Tourani M, Rahmani A, Baee M, Shirafkan F, et al. Pathophysiological roles of chronic low-grade inflammation mediators in polycystic ovary syndrome. J Cell Physiol. 2021;236(2):824–38.
8. Cutillas-Tolín A, Arense-Gonzalo JJ, Mendiola J, Adoamnei E, Navarro-Lafuente F, Sánchez-Ferrer ML, et al. Are dietary indices associated with polycystic ovary syndrome and its phenotypes? A preliminary study. Nutrients. 2021;13(2):313.
9. Karamali M, Kashanian M, Alaeinasab S, Asemi Z. The effect of dietary soy intake on weight loss, glycaemic control, lipid profiles and biomarkers of inflammation and oxidative stress in women with polycystic ovary syndrome: a randomised clinical trial. J Hum Nutr Dietetics. 2018;31(4):533–43.
10. Mombaini E, Jafarirad S, Husain D, Haghighizadeh MH, Padfar P. The impact of green tea supplementation on anthropometric indices and inflammatory cytokines in women with polycystic ovary syndrome. Phytother Res. 2017;31(5):747–54.
11. Cespedes EM, Hu FB. Dietary patterns: from nutritional epidemiologic analysis to national guidelines. Oxford University Press; 2015. pp. 899–900.
12. Hosseini MS, Dizavi A, Rostami H, Parastouei K, Esfandiari S. Healthy eating index in women with polycystic ovary syndrome: a case-control study. Int J Reproductive Biomed. 2017;15(9):575–82.
13. Badri-Fariman M, Naeini AA, Mirzaei K, Moeini A, Hosseini M, Bagheri SE, et al. Association between the food security status and dietary patterns with polycystic ovary syndrome (PCOS) in overweight and obese Iranian women: a case-control study. J Ovarian Res. 2021;14:1–14.
14. Barrea L, Arnone A, Annunziata G, Muscogiuri G, Laudisio D, Salzano C, et al. Adherence to the mediterranean diet, dietary patterns and body composition in women with polycystic ovary syndrome (PCOS). Nutrients. 2019;11(10):2278.
15. Xenou M, Gourounti K. Dietary patterns and polycystic ovary syndrome: a systematic review. Maedica. 2021;16(3):516.
16. Vinke PC, Corpeleijn E, Dekker LH, Jacobs DR Jr, Navis G, Kromhout D. Development of the food-based lifelines Diet score (LLDS) and its application in 129,369 lifelines participants. Eur J Clin Nutr. 2018;72(8):1111–9.
17. Vinke PC, Navis G, Kromhout D, Corpeleijn E. Socio-economic disparities in the association of diet quality and type 2 diabetes incidence in the Dutch lifelines cohort. EClinicalMedicine. 2020;19:100252.
18. Vinke PC, Navis G, Kromhout D, Corpeleijn E. Associations of diet quality and all-cause mortality across levels of cardiometabolic health and disease: a 7.6-year prospective analysis from the Dutch lifelines cohort. Diabetes Care. 2021;44(5):1228–35.
19. Mirzababaei A, Sajjadi SF, Ghodoosi N, Pooyan S, Arghavani H, Yekaninejad MS, et al. Relations of major dietary patterns and metabolically unhealthy overweight/obesity phenotypes among Iranian women. Diabetes Metabolic Syndrome: Clin Res Reviews. 2019;13(1):322–31.
20. Blankenberg S, Barbaux S, Tiret L. Adhesion molecules and atherosclerosis. Atherosclerosis. 2003;170(2):191–203.
21. Alavian SM, Esmaillzadeh A, Adibi P, Azadbakht L. Dietary quality indices and biochemical parameters among patients with non alcoholic fatty liver disease (NAFLD). Hepatitis monthly. 2013;13(7).
22. Sohouli MH, Hadizadeh M, Omrani M, Baniasadi M, Sanati V, Zarrati M. Adherence to lifelines diet score (LLDS) is associated with a reduced risk of breast cancer (BrCa): a case-control study. International Journal of Clinical Practice. 2022;2022.
23. Khadem A, Shiraseb F, Mirzababaei A, Ghaffarian-Ensaf R, Mirzaei K. Association of Lifelines Diet Score (LLDS) and metabolically unhealthy overweight/obesity phenotypes in women: a cross-sectional study. BMC Womens Health. 2022;22(1):1–10.

24. Zimorovat A, Moghtaderi F, Amiri M, Raeisi-Dehkordi H, Mohyadini M, Mohammadi M et al. Validity and reproducibility of a semi-quantitative multiple-choice food frequency questionnaire in adults living in central Iran. 2020.
25. Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the international physical activity questionnaire short form (IPAQ-SF): a systematic review. Int J Behav Nutr Phys Activity. 2011;8(1):1–11.
26. Bilginer MC, Tüfekçi D, Günay YE, Oğuzer U, Coşkun H, Üçüncü O et al. Evaluation of insulin resistance measurement methods in patients with polycystic ovary syndrome. Türkiye Diyabet ve Obezite Dergisi. 2022;6(1).
27. Naghshband Z, Kumar L, Mandappa S, Murthy ASN, Malini SS. Visceral adiposity index and lipid accumulation product as diagnostic markers of metabolic syndrome in south indians with polycystic ovary syndrome. J Hum Reproductive Sci. 2021;14(3):234–43.
28. Nazari M, Mirzaie K, Keshavarz S. Association between lifelines Diet score (LLDS) and some novel anthropometric indices, including body roundness index (BRI), a body shape index (ABSI), visceral Adiposity Index (VAI), and body adiposity index (BAI), in Iranian women: a cross-sectional study. BMC Womens Health. 2024;24(1):172.
29. Asemi Z, Esmaillzadeh A. DASH diet, insulin resistance, and serum hs-CRP in polycystic ovary syndrome: a randomized controlled clinical trial. Hormone Metabolic Res = Hormon- und Stoffwechselforschung = Horm et Metab. 2015;47(3):232–8.
30. Kazemi M, Jarrett BY, Vanden Brink H, Lin AW, Hoeger KM, Spandorfer SD et al. Obesity, insulin resistance, and Hyperandrogenism mediate the link between poor Diet Quality and Ovarian Dysmorphology in Reproductive-aged women. Nutrients. 2020;12(7).
31. Azadi-Yazdi M, Karimi-Zarchi M, Salehi-Abargouei A, Fallahzadeh H, Nadjarzadeh A. Effects of Dietary Approach to Stop Hypertension diet on androgens, antioxidant status and body composition in overweight and obese women with polycystic ovary syndrome: a randomised controlled trial. J Hum Nutr Dietetics: Official J Br Diet Association. 2017;30(3):275–83.
32. Eslamian G, Hekmatdoost A. Nutrient patterns and risk of polycystic ovary syndrome. J Reprod Infertility. 2019;20(3):161–8.
33. Panjeshahin A, Ghadiri A, Hosseinzadeh M. Adherence to DASH Dietary Pattern and Polycystic Ovarian Syndrome: A Case-control Study2021.
34. Alomran S, Estrella ED. Effect of Dietary Regimen on the development of polycystic ovary syndrome: a narrative review. Cureus. 2023;15(10):e47569.
35. Barrea L, Marzullo P, Muscogiuri G, Di Somma C, Scacchi M, Orio F, et al. Source and amount of carbohydrate in the diet and inflammation in women with polycystic ovary syndrome. Nutr Res Rev. 2018;31(2):291–301.
36. González F. Nutrient-Induced inflammation in polycystic ovary syndrome: role in the development of metabolic aberration and ovarian dysfunction. Semin Reprod Med. 2015;33(4):276–86.
37. González F, Rote NS, Minium J, Kirwan JP. Increased activation of nuclear factor kappaB triggers inflammation and insulin resistance in polycystic ovary syndrome. J Clin Endocrinol Metab. 2006;91(4):1508–12.
38. Kawai T, Autieri MV, Scalia R. Adipose tissue inflammation and metabolic dysfunction in obesity. Am J Physiol Cell Physiol. 2021;320(3):C375–91.
39. Sam S. Obesity and polycystic ovary syndrome. Obes Manage. 2007;3(2):69–73.
40. Zheltova AA, Kharitonova MV, Iezhitsa IN, Spasov AA. Magnesium deficiency and oxidative stress: an update. BioMedicine. 2016;6(4):20.
41. Yang Y, Gao M, Nie W, Yuan J, Zhang B, Wang Z, et al. Dietary magnesium sulfate supplementation protects heat stress-induced oxidative damage by restoring the activities of anti-oxidative enzymes in broilers. Biol Trace Elem Res. 2012;146(1):53–8.
42. Morais JBS, Severo JS, de Alencar GRR, de Oliveira ARS, Cruz KJC, Marreiro DN, et al. Effect of magnesium supplementation on insulin resistance in humans: a systematic review. Nutrition. 2017;38:54–60.


## Publisher's note