Polycystic Ovary Syndrome and Dietary Patterns in Iran: A Review Study

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ABSTRACT

Background: Polycystic Ovary Syndrome (PCOs) is one of the most common metabolic and endocrine abnormalities among women in reproductive age. In the case of not comprehensive treatment, PCOs can lead to hormonal, metabolic, and fertility disorders. The exact cause of PCOs is still unclear. This disease seems to have a genetic background caused by the interference of several key genes with the environmental factors such as dietary habit and food intake, which play an important role in prevention and treatment of this syndrome. **Methods:** We searched Scopus, PubMed, SID, and Magiran data bases to find the studies conducted in Iran on dietary patterns, dietary intake, food intake, and PCOs published in English. **Results:** The findings showed that decrease of weight and fat intake from total calorie (especially saturated fat and cholesterol), increase of physical activity and intake of dietary fibers can improve this syndrome. Furthermore, DASH diet, increase of the protein/carbohydrate ratio in the diet, the low-calorie diets, or iso-caloric diets with a low glycemic index can also be useful in this regard. **Discussion:** In recent studies, the effects of some healthy diets were studied on PCOs women. A few of these studies were about finding appropriate dietary patterns for PCOs patients, but their number was limited. So, further studies are needed in this regard.

Keywords: *PCOs; Dietary pattern; DASH diet; Oxidative stress; Visceral adiposity.*

Introduction

Polycystic Ovary Syndrome (PCOs) is a multifactorial and multigenic disorder. It is also one of the most common metabolic and endocrine abnormalities among women in reproductive age, with a prevalence of 7–15 percent in Iran (Azadi-Yazdi *et al.*, 2017). The

National Institute of Child Health and Human Disease (NIH)) as well as Rotterdam and Androgen Excess Society (AES) are commonly used to evaluate the prevalence of PCOs. However, Rotterdam is more common today (Jalilian *et al.*, 2015). Diagnostic criteria suggested by Rotterdam

include the presence of two of the three diagnostic criteria:

● Oligomenorrhea or amenorrhea associated with decreased ovulation. The most common cause of anovulatory infertility is PCOs.

● Hyperandrogenaemia or clinical features of androgen excess, in the absence of other underlying disease states.

● Abnormal ovarian ultrasound with ≥ 12 follicles in each ovary having a diameter of 2 – 9 mm, or increased ovarian volume (Farshchi *et al.*, 2007).

In the absence of treatment, PCOs can cause fertility problems such as infertility, impaired hemorrhage, endometrial carcinoma, depression, low self-confidence, anxiety and sleep apnea, sexual function abnormalities, metabolic disorders such as obesity, Impaired glucose tolerance, type 2 diabetes, hypertension and, and hypertension (Goodarzi *et al.*, 2011, Palomba *et al.*, 2015, Pastore *et al.*, 2011, Wang *et al.*, 2011). It also can lead to abortion by increasing levels of LH, insulin, obesity, as well as increased risk of gestational diabetes mellitus (GDM), lipid profiles, and biomarkers of oxidative stress. One of the common characteristics of PCOs is obesity. Many studies reported that 5-10 percent weight loss can reduce the risk of cardiovascular diseases, type 2 diabetes, endocrine, and reproductive parameters in PCOs women (Faghfoori *et al.*, 2017).

Commonly used treatments include consumption of clomiphene, oral contraceptives, gonadotropins, GnRH agonists, co-utilization of vitamin D and calcium, as well as use of weight loss diets. In resistant cases, laparoscopy is required (Carmina *et al.*, 2016, Cree-Green, 2017, Kalem *et al.*, 2017). Insulin resistance is a major factor in pathogenesis of PCOs (Palomba *et al.*, 2015). Therefore, extensive use of insulin lowering drugs such as metformin is recommended to treat this syndrome. Furthermore, recent studies indicated that some minerals can have positive effects on PCOs or complications of this syndrome: positive effects of chromium on insulin sensitivity (Amr and Abdel-Rahim, 2015), magnesium and selenium on serum testosterone

level, as well as double bond unsaturated fatty acids such as omega-3 on risk factors of metabolic syndrome (Faghfoori *et al.*, 2017). Many studies recommended decrease of weight, intake of fat from total calories (especially saturated fat and cholesterol), increase of physical activity, intake of dietary fibers, and change of diets. The investigated diets to improve this syndrome included increase of the protein/carbohydrate ratio (Sorensen *et al.*, 2012), intake of high protein and low glycemic load (LGL) foods, low glycemic index (LGI) diets, low calorie diets (Love *et al.*, 2016), and an iso-caloric diet with a LGI. In recent years, some researches were conducted over the healthy dietary patterns in women with PCOs. A few of these studies tried to find appropriate dietary patterns for this syndrome. In the present research, we only included the studies appropriate on dietary patterns for women with PCOs conducted over recent years in Iran.

Materials and Methods

We searched the databases of PubMed, Scopus, ISI Web of Science, SID, Magiran, and Google scholar to find the studies written in English conducted on dietary patterns, dietary intake, food intake, and PCOs in Iran. We searched the studies published up to June 2017.

In order to conduct the search, we used the title/abstract, MeSH terms, and other related key words including (dietary pattern OR dietary intake) AND (polycystic ovary syndrome OR PCOs) as well as other related words. In addition to the mentioned databases, we conducted manual search over all eligible original articles, reviews, and other relevant articles.

Results

Table 1 shows the descriptive data of all seven studies. In the following sections, we represent the studies conducted over each category of subjects. Dietary approach for stopped hypertension (DASH) diet and weight loss, anti-mullerian hormone (AMH), metabolic profiles, androgens, body composition, and antioxidant effect in women with PCOs**.**

A randomized clinical trial study was designed

to evaluate the effects of the DASH diet on weight loss, AMH, and metabolic profiles in women with PCOs (Foroozanfard *et al.*, 2017). To this point, 60 overweight or obese women with PCOs were studies; 30 participants were in DASH diet group and 30 in control group. The DASH and control diets consisted of 52-55 percent carbohydrates, 16-18 percent proteins, and 30 percent total fats. The DASH diet was rich in fruits, vegetables, whole grains, low-fat, low cholesterol dairy products, refined grains, and sodium levels less than 2400 mg per day. The amounts of calories' intake were equal in both groups. These results were obtained after 12 weeks: participants had significant reduction in body mass index (BMI) (1.6 ± 0.5 vs. -1.2 ± 0.7 kg/m^2, $P = 0.02$), AMH (-1.1 ± 3.1 vs. 0.3 ± 0.7 ng/mL, $P = 0.01$), malondialdehyde (MDA) (-0.5 ± 0.4 vs. 0.2 ± 0.3 μmol/L, $P < 0.001$), homeostasis model of assessment-estimated insulin resistance HOMA-IR, HOMA-B (-0.9 ± 2.0 vs. -0.1 ± 1.0, $P = 0.02$), and free androgen index (FAI) (-0.03 ± 0.09 vs. 0.06 ± 0.21, $P = 0.02$). However, the DASH group had significant increase in quantitative insulin sensitivity check index (0.01 ± 0.03 vs. 0.004 ± 0.01, $P = 0.02$), sex hormone-binding globulin (SHBG) (3.7 ± 8.5 vs. -1.5 ± 7.2 nmol/L, $P = 0.01$), and nitric oxide (NO) (9.0 ± 4.9 vs. 0.6 ± 2.3 μmol/L, $P < 0.001$) compared with the control group. After adjustment for the baseline values of biochemical variable, BMI, and age, the findings were not influenced.

The other study was a randomized controlled trial over DASH diet, androgens, antioxidant status, and body composition in overweight and obese women with PCOs (Azadi-Yazdi *et al.*, 2017). In a period of 3 months, PCOs was diagnosed in 60 women with overweight or obesity aged 20-40 years (BMI: 25-40) according to the Rotterdam criteria. Anthropometric characteristics, dietary intake, and serum androgens were measured at the beginning and at the end of the study. Initial results showed differences in testosterone and the secondary outcomes included changes in androstenedione, (SHBG: Sex hormone-binding globulin), total antioxidant capacity, and body composition. The combination of macronutrients was similar in interventional and control groups, containing 50-55 percent carbohydrates, 15-20 percent protein, and 25-30 percent total fat. People were asked to write their 3-day food recall (two days of week days and one day in weekend) per month. The comparison between the two groups indicated a significant decrease in BMI, body mass, and serum androstenedione. Furthermore, concentrations of SHBG and free androgen index and 2,2′-diphenyl-1-picryylhydrazyl (DPPH) scavenging activity increased in the DASH group compared to the control group. After adjusting for the potential confounding variables, the researcher reported that these differences were not significant.

Therefore, we can conclude that: DASH diet have high amount of antioxidant content and this dietary pattern may have beneficial effects on reduction of BMI, MDA, insulin resistance, free androgen index (FAI), and serum androstenedione. It also can have incremental effects on insulin sensitivity, SHBG, and NO in women with PCOs.

As mentioned before, DASH diet contains high amounts of total dietary fiber, phytoestrogens, antioxidants, isoflavones, magnesium, and calcium that have good effect on oxidative stress and serum hs-CRP. Moreover, intake of both antioxidants and magnesium was inversely associated with insulin resistance. Two studies were conducted in this regard:

Overweight or obese women with BMI ≥ 25 kg/m^2 in the age range of 18-40 years were diagnosed with PCOs according to the Rotterdam criteria.

The selected participants were categorized into two groups: 24 in the DASH diet and 24 in the control group. The DASH and control diets consisted of 52 percent carbohydrates, and 18 percent proteins, 30 percent total fats. . As a result, the researchers found a significant decrease in participants' weight (4.4 vs. -1.5 kg; $P < 0.001$), BMI (-1.7 vs. -0.6 kg/m^2; $P < 0.001$), serum triglyceride (TG) (-10.0 vs. +19.2 mg/dL; $P = 0.005$), and VLDL-c levels (-2.0 vs. 3.9 mg/dL; $P = 0.005$). However, the concentrations of

total antioxidant capacity (TAC) (+98.6 vs. 174.8 mmol/L; $P < 0.001$) and total glutathione (GSH) (+66.4 vs. -155.6 μmol/L; $P = 0.005$) increased in the DASH group compared with the control group. After adjustment for weight, TG (-5.9 ± 7.5 vs. 15.2 ± 7.5 mg/dL, $P = 0.07$) and VLDL-c levels (-1.2 ± 1.5 vs. 3.0 ± 1.5 mg/dL, $P = 0.07$) reduced in the DASH group (Asemi *et al.*, 2014).

Regarding the insulin resistance and serum hs-CRP, the study showed a significant reduction in serum insulin levels (−1.88 vs .2.89 μIU/mL, $P = 0.03$), HOMA-IR score (−0.45 vs. 0.80; $P = 0.01$), and serum hs-CRP levels (−763.29 vs. 665.95 ng/mL, $P = 0.009$) in DASH group. Furthermore, the waist size (-5.2 vs.-2.1cm; $P = 0.003$) and hip circumference (-5.9 vs. -1 cm; $P < 0.0001$) reduced in DASH group compared with the control group. No significant differences were observed in the mean changes of fasting plasma glucose and HOMA-B between the two groups. After adjusting for age and the baseline weight measure, no significant changes were reported in the findings. After adjustment for the baseline values of biomarkers, a significant difference was seen in quantitative insulin sensitivity check index (QUICKI) between the two groups (0.02 vs. −0.01, $P = 0.04$) (Asemi and Esmaillzadeh, 2015).

So, we found that the DASH diet could be an appropriate dietary pattern for women with PCOs. In recent years, some studies were conducted to evaluate and compare the dietary intakes of women with PCOs and healthy women. These studies also determined the relationship of the dietary patterns with cardiometabolic risk factors in women with PCOs in Iran.

Dietary intake in PCOs and healthy women: To achieve the difference between the dietary intake of PCOs and healthy women, a case-control study was conducted on 142 women with PCOs and 140 eumenorrheic non hirsute women (age and BMI were matched between the two study groups). In this study, the dietary intakes of the two groups were compared using a validated Food Frequency Questionnaire (FFQ). The findings showed that energy and macronutrient intakes were almost the

same between the women with PCOs and the controls. Women with PCOs had significantly higher weight measures (case: 69.37 ± 14.97, control: 67.45 ± 12.92, $P = 0.048$) and hip circumferences (case: 104.9 ± 10.1, control: 101.5 ± 10.73, $P = 0.007$), but they had lower waist/hip ratio in comparison with the control group (case: 0.80 ± 0.73, control: 0.83 ± 0.09, $P = 0.031$). Consumption of high GI food items and egg in PCOs women was significantly higher than the controls, but intakes of vegetable and legume were significantly lower in PCOs women ($P < 0.05$) (Shishehgar *et al.*, 2016).

Anthropometric characteristics and dietary patterns in women with PCOs: Recently, the researchers concluded that the dietary intake of women with PCOs should be determined. Therefore, a case-control study was conducted on 65 women with PCOs and 65 age-matched healthy women in 2013. Demographic, anthropometric, and dietary intake data were collected from each group and the results were compared. No significant difference was observed between the mean of the BMI of the two groups, but in PCOs group the mean of waist circumference was significantly higher than the control group ($P = 0.016$). Consumption of calories and fat was significantly higher In PCOs women and the frequency of overweight patients with hirsutism was higher in PCOs group (Ahmadi *et al.*, 2013).

This study was only about the food and dietary intakes in women with PCOs compared with the healthy women. So, it did not investigate the dietary patterns.

Dietary pattern and cardiometabolic risk factors in women with PCOs: A case- control study was conducted on 53 women with PCOs and 167 age-matched healthy women in 2017. The participants were selected from the population of Tehran lipid and glucose study. Dietary intakes were collected using a semi-quantitative FFQ. The relationship between the dietary patterns and cardiometabolic risks was investigated by Pearson's correlation and linear regression. The dietary pattern was characterized by high consumption of fried

vegetables, vegetable oils (except olive oil), salty snacks, legumes, eggs, fast foods, onion, and garlic. However, it was defined with low intakes of traditional sweets, high fat dairy, low fat dairy, cruciferous vegetables, sugars, and honey, which had positive correlation with visceral adiposity index (VAI). Consumption of this dietary pattern had a significant association with higher TG and TG/HDL-c ratio as well as lower HDL-c in both groups. A positive correlation was also found for systolic blood pressure, waist circumference, total cholesterol (TC), and LDL-c in the control group. After adjusting for BMI and age, dietary pattern had an association with TG and TG/HDL-c in both groups. Compliance with this dietary pattern in the control group indicated a higher correlation with the cardio-metabolic risk in comparison with the PCOs group (Ehsani *et al.*, 2016). The purpose of this study was to identify the VAI prediction model using a reduced rank regression. Moreover, it aimed to examine its associations with cardiometabolic risks in women with PCOs.

Table 1. Characteristics of included studies

First author	Study design, Duration	Study population	Outcome
Foroozanfard, et al. 2017	RCT, 12 weeks	30 DASH Group 30 control Group	Significant reduction in BMI, AMH, MDA, HOMA-IR, HOMA-B, but increase in QUICK, serum SHBG, NO in DASH diet group.
Azadi-Yazdi, et al. 2016	RCT, 3 months	60 PCOS women 30 DASH group 30 control group	Significant reduction in weight, BMI, fat mass and serum androstenediones. Increase in SHBG and DPPH scavenging activity in Dash compare to control group.
Asemi, et al. 2015	RCT, 8 weeks	48 PCOs women , 24 DASH diet, 24 control	Significant reduction in waist, hip circumference, serum insulin, HOMA-IR, serum hs-CRP in DASH diet group and no significant differences in mean changes of FPG and HOMA-B in both DASH and control groups.
Asemi, et al. 2014	RCT, 8 weeks	48 PCOs women 24 DASH diet 24 control	Significant reduction in weight, BMI, TG and VLDL-c and significant increase in plasma total GSH and TAC in DASH compare to control group.
Shishehgar, et al. 2016	CC	142 PCOs women 140 amenorrhea non hirsute, BMI and age matched	Dietary pattern of PCOs women contain high glycemic index food items and low legumes and vegetables
Ehsani, et al. 2017	CC	53 PCOs women 167 age-matched healthy women	Consumption dietary pattern (high in fried vegetables, vegetable oils except for olive oil and fast foods and low consumption of dairy and cruciferous vegetables) had significant association with higher systolic blood pressure, WC, TC and LDL-c in control group. After adjustment for age and BMI, dietary pattern was associated with increase in TG and TG/HDL-c in both groups.
Ahmadi, et al. 2013	CC	65 PCOs women 65 age-matched healthy women	PCOs women consumed more calories and fat than healthy women. No significant difference for BMI in two groups, WC was significantly higher in the PCOs group.

DASH: Dietary approach stopped hypertension; RCT: Randomized clinical trial; CC: Case- control; PCOs: Polycystic ovary syndrome; BMI: Body mass index;AMH:Anti-mullerian; MDA: malondialdehyde; HOMA-IR: assessment-estimated insulin resistance; NO: Nitric oxide; FPG: Fasting plasma glucose; QUICK: Quantitative Insulin sensitivity Check index; SHBG: Sex hormone binding protein; DPPH: 2,2'- diphenyl- 1- picryylhydrazyl; HOMA-IR: Homeostasis model of assessment insulin Resistance; hs-CRP: high-sensitivity C-reactive protein; HOMA-B: Homeostatic model assessment-beta cell function; TG: Triglycerides; VLDL-c: Very low-density lipoprotein; TAC: Total antioxidant capacityGSH: Total glutathione; WC: Waist circumference; TC: Total cholesterol; LDL-c: Low-density lipoprotein; HDL-c: High-density lipoprotein

Discussion

The researchers concluded that some of the dietary patterns might be appropriate to treat PCOs. In recent studies, some healthy diets such as DASH diet were prescribed to the PCOs women. DASH diet is a low-glycemic-index low-energy dense diet rich in fruits, vegetables, whole grains, and low-fat dairy products, but low in saturated fats, cholesterol, refined grains, and sweets. This eating plan was initially proposed for the management of hypertension (Vollmer *et al.*, 2001). It also showed beneficial effects on type 2 diabetes (Azadbakht *et al.*, 2011), gestational diabetes (Asemi *et al.*, 2013), inflammatory factors (Soltani *et al.*, 2016), metabolic syndrome (Esposito and Giugliano, 2006), and non-alcoholic fatty liver disease (NAFLD) (Razavi Zade *et al.*, 2016). This dietary pattern contains high amounts of dietary fiber, phytoestrogens, antioxidants, isoflavones, magnesium, and calcium, along with its LGI (Ahmadi *et al.*, 2013) . Regarding this diet, antioxidants and magnesium intake were inversely associated with insulin resistance (Puchau *et al.*, 2010). Moreover, DASH diet contains high antioxidants and arginine amino acids that may improve metabolic status using the decreased NADPH oxidase activity and reduced level of angiotensin II (Chen *et al.*, 2001). On the other hand, increased intake of micronutrients, such as calcium in DASH diet would result in fecal fat excrete, weight loss, and increased insulin

sensitivity (Onakpoya *et al.*, 2011). Furthermore, weight reduction might reduce testosterone levels (Luo and Xu, 2012). Nevertheless, this dietary pattern seems to be potentially beneficial for women with PCOS.

In recent years, very limited number of studies was conducted to find an appropriate dietary pattern for women with PCOS. So, further studies are needed to investigate the effective dietary patterns in PCOS women for treatment and reduction of this syndrome and its complications.

Conclusion

Studies concluded that diet modification such as DASH diet, increase of the protein/carbohydrate ratio in the diet, the low calorie diets, or iso-caloric diets with a low glycemic index may have beneficial effects in treatment of women with PCOS. However, studies which conducted on finding appropriate dietary pattern for this syndrome are limited and Future Studies are required to finding major dietary pattern in women with PCOS.

Authors' contribution

All authors participated to designing, developing the search strategy and writing the manuscript. Panjeshahin A and Khosravi M conducted the systematic search and study selection; all authors read and approved the final manuscript.

Conflict of interest

There is not any conflict of interest.

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