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Evaluation of the Relationship between Insulin Resistance and Macronutrient Intake in Four Subgroups of Polycystic Ovary Syndrome (PCOS) based on Rotterdam Diagnostic Criteria

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Abstract

Introduction: Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder in women of reproductive age. It is linked to genetic and environmental factors such as nutrition. Insulin resistance is one of the major pathological changes in PCOS. This study aimed to determine the relationship between insulin resistance and macronutrient intake in PCOS subgroups.

Methods: *In vitro* and clinical studies and completing 168-items PPQ Frequency Questionnaire were conducted for all macronutrients.

Results: There was a significant relationship between HOMA-IR and some dietary components ($P<0.05$). (Increased calorie in group A, increased total fat intake in group C, lower intake of unsaturated fats (PUFA and MUFA) in group D and higher intake of Saturated Fat (SFA) and protein intake in control group). There was no correlation in subgroup B (ovulatory phenotype).

Conclusion: Due to the significant relationship between insulin resistance and some dietary components in PCOS subtypes, it is recommended to maintain a balance in carbohydrate and fatty acids intake, increasing dietary fiber to improve health parameters in PCOS subjects.

Keywords: Nutrition; Polycystic Ovary Syndrome; Insulin Resistance

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Abbreviations

PCOS: Polycystic Ovary Syndrome; ESHRE: European Society of Human Reproduction and Embryology; FFQ: Food Frequency Questionnaire; HOMA: Homeostasis Model Assessment Method; HOMA-IR Insulin Resistance calculated by the Homeostasis Model Assessment Method; FG: Ferrimen-Gallweyscore, FAI: Free Androgen Index; SHBG: Sex Hormone Binding Globulin; TT: Total Testosterone, GI: Glycemic Index, PUFA: Polyunsaturated Fatty Acids; MUFA: Multiple Polyunsaturated Fatty Acids; SFA: Saturated Fatty Acids

Introduction

Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder in women [1]. One of the most commonly used definitions for PCOS is the presence of at least two of the three clinical biochemical criteria of Rotterdam. These symptoms of hyperandrogenemia, oligomenorrhea or ovulation, and macroscopic ultrasound evidence that the size of the ovaries in these women is 2 to 5 times the normal range and the ovaries contain numerous cysts that are typically less than one centimeter in diameter [2,3]. The syndrome may occur with some or all of the symptoms, menstrual disorders, infertility, hirsutism, acne and alopecia [4]. The prevalence of PCOS due to different clinical features and biochemical characteristics of these patients has been reported different in several studies according to the race, ethnicity and the study population [5]. In a study by Gabriel et al. [6] in Brazil, the prevalence of polycystic ovary syndrome was estimated to be 32% among 859 women between the ages of 18 and 45 years. In a study by Ramazan et al. [7] in Iran, its prevalence was estimated at 14.6% according to the Rotterdam criteria. This syndrome is associated with a wide range of reproductive, metabolic, and psychological disorders [8]. In 2004, the cost of treatment in the US health care system was estimated to be approximately $4 billion; 40% of which was for

women with insulin resistance PCOS and type 2 diabetic women; and its management, especially in people with insulin resistance PCOS, is very important [9]. The most well-known cause of the pathogenesis of polycystic ovary syndrome is insulin resistance [10]. Insulin resistance is a central pathogenic factor that occurs during the development of hyperinsulinemia and is a cardiometabolic disorder that stimulates all tissues and increases the abnormality in the process of ovarian steroidogenesis. Therefore, insulin resistance in patients with polycystic ovary compared to healthy women may increase the risk of diabetes mellitus, dyslipidemia, atherosclerosis and cardiovascular disease [11,12]. Its pathophysiology is not fully understood, although several hypotheses have been proposed, malformations in four endocrine active components including the ovary, renal gland, hypothalamic-pituitary axis, and insulin-sensitive tissues such as the insulin [13]. Both lean and obese women with PCOS are susceptible to insulin resistance, but obese women are more susceptible [14]. Obesity can act as a gonadotropin due to insulin resistance, impairing the synthesis of androgens, or through adipocytokines, through direct or indirect effects on adipose tissue. It can also affect the peripheral metabolism of steroids [15]. Therefore, changes in lifestyle and weight loss through exercise and nutrition are recommended for these patients [9]. In the study of Thomson et al. [16], weight loss of 9 kg over 20 weeks in overweight and obese individuals with PCOS led to a significant decrease in fasting insulin, IR-HOMA, testosterone, free androgen specificity (FAI), increased Sex Hormone-Binding Globulin (SHBG) and improved fertility [16]. In nutrition science, macronutrients are divided into three broad categories, including protein, carbohydrate, and fat. The major role of macronutrients is to provide energy in units of calories [17]. Some studies have shown that protein, carbohydrate and fat intake can exacerbate insulin resistance [18-21]. Some studies also reported that high protein, high carbohydrate, and fat-rich diets reduced insulin resistance or had no effect on insulin resistance [22-25]. PCOS is highly prevalent. It has adverse effects on reproduction, metabolic status, diseases such as diabetes, cardiovascular disease, and endometrial cancer. Given the many unknowns about this disease, efforts to clarify the causes, mechanisms, possible prevention, treatment and improvement of patients' quality of life seem necessary. Since nutritional behaviors play a major role in human health or disease, it is important to examine the relationship between nutrition and PCOS. On the other hand, inconsistencies in previous studies led researchers to design and execute an article aimed at "determining the relationship between insulin resistance and macronutrient intake in four subgroups of the PCOS phenotype based on Rotterdam criteria".

Methods

The present study is a case-control study to investigating dietary intake of micronutrients in four subgroups of polycystic ovary syndrome and control group with insulin resistance in Tehran during 2015 to 2016. The sample size based on the results of the pilot study and the correlation between insulin resistance index and dietary component showed that the minimum correlation between these indices was 0.50. Therefore, with 95% confidence and 80% test power, the number of samples required was 26.2 based on the following formula for each subgroup with approximately 27 considered. Considering 20% of sample loss, the final volume per phenotype was estimated at 31 individuals.

$$n=\frac{(z_{1-\frac{\alpha}{2}}+z_{1-\beta})^2}{(c(r))^2}+3$$

$$C(r)=\frac{1}{2}\log_e\frac{1+r}{1-r}=\frac{1}{2}\log_e\frac{1+0.5}{1-0.5}=0.55$$

$$n=\frac{(1.96+0.84)^2}{(0.55)^2}+3=26.2\cong 27$$

$$27 + 0.022(27) = 31$$

The sampling method was available. Subjects were selected from referrals to gynecology ward, endocrinology ward of Arash Hospital and selected private clinic if they were eligible to enter our study after filling informed consent. Inclusion criteria in the case group were: Iranian race, age 18 to 40 years, lack of chronic metabolic and non-metabolic diseases affecting diet such as diabetes mellitus, hyperthyroidism, hypothyroidism, and hyperlipidemia, not taking medicines that affect appetite and diet, no specific diet, no pregnancy, no hormone use for three months before starting the study. In the event of any problems, including pregnancy and illness requiring specific drug use, the research units were excluded. Inclusion criteria in the control group were: 18 to 40 years old and without any diagnostic criteria for PCOS (non-hirsute: without excessive hair growth, with regular ovulation cycles) referred to Women's Clinic for other reasons. Then the two groups were matched for education, BMI, economic status, and physical activity and exercise status. Initially, the disease was diagnosed after excluding other abnormalities that mimic the PCOS phenotype) ovarian or adrenal neoplasm, Cushing's syndrome, hyperprolactinemia, thyroid disease and congenital adrenal hyperplasia starting in adulthood (AOAH)) by assessing 17OHP, DHEAS, cortisol, thyroid hormones, and prolactin levels. Then based on the Rotterdam diagnostic criteria, two of the following three disorders are necessary:

Clinical hyperandrogenism (Hirsutism) (H)

Clinical Hyperandrogenism= The Ferriman Gallwey score of 8, and above or biochemical hyperandrogenism= elevated serum total testosterone levels or Free Androgen Index (FAI)): Hyperandrogenic serum Total Testosterone (TT), greater than 0.68 ng/ml and Free Androgen Index (FAI) More than 5.36% [26,27]. The TB and SHBG assay methods were measured by electro quantitative luminescence using a Roche German kit by Cobas E 411. FAI= TT (nmol/l)/SHBG (nmol/l)*100 [28].

Ovulation disorder: (Oligo/anovulation)

The menstrual cycle of more than 35 days (oligomenorrhea) or more than 3 months (amenorrhea) [29].

Polycystic ovary view in ultrasound (P)

An ovarian volume greater than 10 cubic centimeters in at least one ovary or observation of more than 5 to 8 multiple fine follicles [29]. After entering the study, they were divided into the following four phenotypes [30]:

1. Complete phenotype or A (H+P+O)
2. Ovulatory phenotype or B (H+P)
3. Normoandrogenic phenotype or C (P+O)
4. Phenotype or D (H + O)

Finally, 182 participants were included in the study (31 people in control group, 41 people in group A, 33 people in group B, 40 people in group C, and 37 people in group D). The researcher assessed physical activity by asking research units about whether or not to exercise. Participants' physical activity was measured at three levels

Table 1: Comparison of demographic components at baseline.

Demographic Components	Phenotype A: H + O + P N=41	Phenotype B: H + P N=33	Phenotype C: O + P N=40	Phenotype D: H + O N=37	Control group N=31	P -value
Age	28.07 ± 4.70	27.00 ± 5.44	29.70 ± 6.44	29.83 ± 5.93	28.07 ± 4.70	0.099 K.W
BMI	25.48 ± 5.23	25.06 ± 4.28	25.08 ± 3.93	24.98 ± 4.80	25.48 ± 5.23	0.99 K.W
Educational Status						
Under the Diploma	4 (9.8)	3 (9.1)	4 (10.0)	2 (5.4)	2 (6.5)	0.309 Chi-square
Graduate Diploma/ Diploma	9 (22.0)	5 (15.2)	10 (25.0)	15 (43.2)	14 (45.2)	
Bachelor	19 (46.3)	16 (48.5)	20 (50.0)	16 (40.5)	10 (32.3)	
Masters degree and higher	9 (22.0)	9 (27.3)	6 (15.0)	4 (10.8)	5 (16.1)	
Economic Situation						
Poor	16 (39.0)	23 (69.7)	23 (57.5)	21 (56.8)	17 (54.8)	0.275 Chi-square
Medium	16 (39.0)	5 (15.2)	11 (27.5)	7 (18.9)	7 (22.6)	
Good	9 (22.0)	5 (15.2)	6 (15.0)	9 (24.3)	7 (22.6)	
Physical Activity Status						
Level 1	23 (56.1)	20 (60.6)	25 (62.5)	25 (67.6)	20 (67.6)	0.871 Chi-square
Level 2	6 (14.6)	6 (18.2)	7 (17.5)	5 (13.5)	5 (13.5)	
Level 3	12 (29.3)	7 (21.2)	8 (20.0)	7 (18.9)	6 (18.9)	

H: Clinical +/Paraclinical Hyperandrogenism; **O:** Oliogo/Anovulation; **P:** Pco sonographic view

based on their responses. Level 1: Normal daily activities without exercise, Level 2: Moderate physical activity: (1 to 2 times a week, each time for at least 20 min). High physical activity: (3 or more 3 times a week, each time for at least 20 min) [31]. For all samples, the 168 items Food Frequency Questionnaire (FFQ) was completed. Validity and reliability have been evaluated by Asghari, Isfahani, Mirmiran et al. [32,33]. This questionnaire was used to obtain a person's usual diet during the past year. This questionnaire includes all food groups breads, rice, pasta, cereals, dairy (milk, yogurt, buttermilk, cheese, whey, and ice cream), meat group (lamb, beef, minced and sliced, fish, poultry), group of vegetables (leafy and non-leafy vegetables), group of fruits (all kinds of fruits and juices), group of oils, all kinds of sweets, nuts, noodles, canned foods, beans, tea and coffee, it is soda and eggs. In order to analyze the nutritional information of the FFQ questionnaire, Excel-based software was used to analyze nutrient intakes. (Includes formulas formulated and programmed in Excel in which the nutrients of the food frequency questionnaire are broken down into micronutrients). In the program above, for each micronutrient of each nutrient, a function is defined based on the amount of nutrients in one gram of each nutrient. Thus, by entering the amount of grams consumed in each food item in its respective cell, Excel calculated the number of nutrients in the germ consumed in that nutrient. Finally, the total amount of nutrients consumed by each individual is obtained from the sum of all the nutrients in each food item consumed [34]. Given the different daily calorie intake of each individual, it is obvious that the ratio of each nutrient to the total daily calorie intake and consequently the contribution of one nutrient to the total calorie intake may also be different. Therefore, in order to make an accurate comparison between the information obtained from each individual with the other participants, after caloric intake of each of these macronutrients daily; we calibrated them all for energy adjusting. Finally, the whole analysis was performed on the energy regulated data. Anthropometric evaluations (height, weight, BMI), ovarian sonography, hirsutism as a clinical symptom of hyperandrogenism, hormonal tests were performed to determine serum androgens. Questions were raised about menstruation. Menstrual disorder was evaluated. The macronutrients to be measured fat (Total Fat, Saturated Fatty Acids (SFA), Polyunsaturated Fatty Acid (PUFA), Monounsaturated Fatty Acids (MUFA), calories, protein and total and soluble fiber. In this study, insulin resistance was assessed using HOMA index. The original HOMA model was described in 1985 with a formula for approximate estimation by Mathew et al. [35]. The formula of the HOMA index is calculated by multiplying the fasting blood glucose concentration (mmol/l) and the fasting insulin concentration (mmol/ml) Divide by a fixed number of 22.5 (using fasting serum glucose and fasting insulin levels). The cut off point for defining insulin resistance is considered based on the HOMA-IR criterion (cut off >2.5) [36]. HOMA-IR= fasting glucose (μU/ml) × fasting insulin (mmol/l)/22.5. The 5 ml of venous blood (to check fasting blood glucose and insulin levels) were obtained from all research units in the laboratory and in the fasting state. Glucose was measured by glucose oxidase assay and insulin was measured by immunoradiometric method. Beck Man's immunotech kit was used to check the cases, with an extra-test accuracy of 3.4% and an intra-test accuracy of 4.3%. SPSS software was used for data analysis and statistical tests. At first, Kolmogorov-Smirnov test was used for data normality. Parametric tests (for normal data) and non-parametric tests (for non-normal data) were used to analyze the data. Kruskal Wallis test (for non-normal data) and one-way ANOVA test (for normal data) were used to compare the variables. Spearman correlation test (because data were not normal) was used to investigate the relationship between quantitative variables. Chi-square test was also used to investigate some underlying variables. Significance level P<0.05 was considered.

Results

The results of Kruskal Wallis, one-way ANOVA and Chi-square tests showed that there were no significant differences between the four subgroups of PCOS women and the control group in terms of age (P=0.099), body mass index (P=0.990), education level (P=0.309), economic status (P=0.275), and physical activity status (P=0.871). The two groups were homogeneous (p>0.05) (Table 1). Insulin resistance status was compared with the HOMA-IR index (Cut off >2.5) in PCOS and control groups with the Chi-square test. There

Table 2: Comparison of Insulin Resistance Status with HOMA-IR Index in PCOS Subgroups and Control group.

PCOS Subtypes										
	Phenotype A		Phenotype B		Phenotype C		Phenotype D		Control Group	
Insulin resistance	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
HOMA-IR ≤ 2.5 NO	16	39.5	16	48.5	25	62.5	19	51.4	29	93.5
HOMA-IR>2.5#	25	61	17	51.5	15	37.5	18	48.6	2	6.5
Total	41	100	33	100	40	100	37	100	31	100
P -value	P<0.001 Chi-square									

#Cut off >2.5

Table 3: Correlation between dietary components and HOMA insulin resistance index in four subgroups of PCOS and control group.

Evaluation of correlation between dietary components and HOMA insulin resistance index in subgroup A (H+P+ O)									
Nutritional		Calories	Total Fiber	Soluble Fiber	Total Fat	PUFA	MUFA	SFA	Protein
HOMA-IR	R	0.334	-0.188	-0.139	0.195	181	-0.151	0.01	0.017
	P	0.033	0.24	0.385	0.227	0.264	0.352	0.952	0.916
Evaluation of correlation between dietary components and HOMA insulin resistance index in subgroup B (H+P)									
Nutritional		Calories	Total Fiber	Soluble Fiber	Total Fat	PUFA	MUFA	SFA	Protein
HOMA-IR	R	0.019	0.309	0.288	-0.173	0.094	-0.069	-0.051	-0.037
	P	0.915	0.08	0.104	0.337	0.604	0.705	0.776	0.836
Evaluation of correlation between dietary components and HOMA insulin resistance index in subgroup C (P+O)									
Nutritional		Calories	Total Fiber	Soluble Fiber	Total Fat	PUFA	MUFA	SFA	Protein
HOMA-IR	R	0.074	0.036	-0.035	0.341	0.226	0.256	0.053	-0.063
	P	0.649	0.824	0.83	0.031	0.161	0.11	0.747	0.697
Evaluation of correlation between dietary components and HOMA insulin resistance index in subgroup D (H+O)									
Nutritional		Calories	Total Fiber	Soluble Fiber	Total Fat	PUFA	MUFA	SFA	Protein
HOMA-IR	R	-0.028	-0.288	-0.132	0.124	-0.404	-0.473	0.062	-0.311
	P	0.033	0.24	0.385	0.227	0.013	0.003	0.004	0.061
Evaluation of correlation between dietary components and HOMA insulin resistance index in Control group									
Nutritional		Calories	Total Fiber	Soluble Fiber	Total Fat	PUFA	MUFA	SFA	Protein
HOMA-IR	R	0.139	0.247	0.522	0.202	0.482	0.512	0.366	0.443
	P	0.455	181	0.066	0.275	0.067	0.052	0.043	0.012

was a significant difference in the index of insulin. The number of women with polycystic ovary syndrome who also had insulin resistance was higher in phenotype A (complete PCOS phenotype (no ovulation, hirsutism, and sonographic abnormality)) than in other groups (61%) (Table 2). Spearman test results showed that insulin resistance in different PCOS subgroups and control group correlated with the frequency of oral intake of macronutrients. In subgroup A, the HOMA insulin resistance index was significantly correlated with daily calorie intake (P=0.033). In subgroup B, there was no significant relationship between the HOMA insulin resistance index and any of the dietary components (P>0.05). In subgroup C, there was a significant positive relationship between HOMA insulin resistance index and total fat (P=0.031). In subgroup D, there was a significant negative relationship between the HOMA insulin resistance index with Polyunsaturated Fatty Acids (PUFA) (P=0.013) and Multiple Polyunsaturated Fatty Acids (MUFA) (P=0.003) and Saturated Fatty Acids (SFA) (P=0.004). In the control group, there was a significant positive correlation between HOMA insulin resistance index and saturated fatty acids (P=0.043) and protein intake (P=0.012) (Table 3).

Discussion

Many studies have investigated and compared insulin resistance with nutritional factors, but so far no study has investigated the association between insulin resistance and macronutrient intake in four phenotypes of women with PCOS. Due to differences in dietary patterns in different countries, this study investigates the relationship between insulin resistance and nutritional pattern in consumption of macronutrients in Iran. In the present study, macronutrients were evaluated in three broad categories including protein, carbohydrate, and fat with HOMA insulin resistance index. The results showed that insulin resistance in different PCOS subgroups and the control group correlated with the frequency of oral intake of macronutrients. In subgroup A, the HOMA insulin resistance index was correlated with daily calorie intake. In subgroup B, there was no relationship between the HOMA insulin resistance index and any of the dietary components. In subgroup C, there was a positive relationship between HOMA insulin resistance index and total fat. In subgroup D, there was a negative relationship between the HOMA insulin resistance index with Polyunsaturated Fatty Acids (PUFA) and Multiple Polyunsaturated Fatty Acids (MUFA) and Saturated Fatty Acids (SFA). In the control group, there was a positive correlation between HOMA insulin resistance index and saturated fatty acids and protein intake. So far, no study has been found on the intake of macronutrients individually in insulin-resistant PCOS phenotypes. Therefore, the present study is compared with the results of studies evaluating the

association between different dietary components and insulin resistance in these patients. In the Graff study, a correlation was found between dietary glycemic index and insulin resistance in people with the classic PCOS phenotype (phenotypes A and B) [37]. In Pehlivanov's study, people with PCOS in subgroups A and B received more calories and had a higher HOMA insulin resistance index, and these two studies were in line with the present study [18]. A case-control study was conducted by Zhang J et al. [22] in China on 169 PCOS women and 338 control and non-PCOS women who were homogenous in age. The results showed that women with PCOS had lower carbohydrate and calorie intake than controls, which was contrary to the results of the present study. The different results with the present study may be due to differences in culture, nutrition, and taste between different races. Douglas's study included 30 women with PCOS and 27 healthy women who were matched for age, race, and BMI and reported: People with PCOS tend to consume high glycemic index foods, but there was no significant positive association between these foods and insulin resistance [38]. The difference in the results of this study may be due to the lower sample size than the present study. Sjaarda et al. [23] also conducted a study on 259 women with PCOS and reported that there was no association between high carbohydrate diet and high calorie intake or any macronutrients with insulin resistance. The results of this study are contrary to the results of the present study. Ebbeling et al. [39] consider the type of carbohydrate intake more important than its total amount to maintain the metabolic health of women with PCOS. Low glycemic diets improved insulin resistance. Bryneset al. [40] also showed that high glycemic foods had the opposite effect. Insulin Resistance (IR) is the physiological condition during which the insulin hormone is less able to lower blood sugar. The subsequent rise in blood sugar can be so high that it goes beyond the normal range of blood sugar and can be detrimental to health. Some cells, such as fat and muscle cells, require insulin to enter glucose. If these cells do not respond to the circulating insulin, their blood sugar will rise. Insulin resistance has a number of effects, including a decrease in the ability of adipocytes to harvest blood lipids and increased hydrolysis of peripheral triglycerides. This hydrolysis can increase the free fatty acids in the bloodstream. Since the human genotype has not changed over the centuries, environmental factors have been considered as a major contributor to the increase in insulin resistance in recent years. One of the most important issues in this regard is the energy balance between the number of calories consumed through food and the number of calories consumed during physical activity. In addition to energy balance, the type of food consumed is also important. From an evolutionary perspective, it has been suggested that overweight and other related diseases are the natural results of high-calorie intake [41]. Overweight by acting as insulin resistance can act as a gonadotropin and thereby impair the synthesis of androgens. Overweight can also affect the hypothalamus and ovaries through adipocytokines, indirectly or indirectly, and ultimately affect the peripheral metabolism of steroids. Therefore, as the first line of treatment for women with PCOS, the amount of calorie intake and weight management should be considered [14]. As in our study, high-calorie intake was associated with insulin resistance in patients with complete PCOS phenotype (Lack of ovulation, hirsutism, and abnormality in the ultrasound view). Consistent with the results of the present study, is the study of Kasim-Karakas, who examined the effects of dietary Polyunsaturated Fatty Acids (PUFA) in 17 patients with PCOS. During a 3rd month diet period, dietary fats were replaced with PUFAs, which reported that PUFAs significantly increased diol 3-glucuronide progeny, thereby reducing insulin resistance and ovulation [19]. Zivkovic et al. [20] reported that diets containing monounsaturated fatty acids with a double bond (MUFA) in women with PCOS decrease insulin resistance. In a study by McLaughlin et al. [42], diets containing MUFA and PUFA lipids reduced insulin resistance in patients with PCOS. In the present study, in subgroup D, an inverse relationship was observed between daily intake of PUFA and MUFA with HOMA insulin resistance index. Inconsistent with the present study is Tierney's study that diets rich in unsaturated fatty acids with a double bond (MUFA) increased insulin resistance [43]. In the He-Xia XIA study, there was a positive correlation between saturated fat intake and HOMA-IR in women with PCO. This study was in line with the present study [24]. Stender et al. [25] conducted a study to determine the effect of trans fatty acids on health; their results showed that high-fat diets, especially saturated fats and trans-fatty acids, were associated with decreased insulin resistance [25]. The results of this study were contrary to the results of the present study. In our study, an increase in saturated fat intake in subgroup D and control was associated with increased insulin resistance. The quality and quantity of fats in the diet composition play an important role in the homeostasis and insulin sensitivity in animals and humans. Some studies have shown that high fat diets can cause hyperglycemia and insulin resistance. Fatty acids with varying degrees of saturation may not be able to induce fat-induced insulin resistance. It seems that the combination of fatty acids or type of fatty may have an independent effect on insulin function and alter insulin sensitivity [44]. In the present study, total fat increased in subgroup C (ovarian dysfunction + abnormality in the ultrasound view) and in subgroup D (hirsutism + ovulation disorder) decreased MUFA and PUFA consumption and increased SFA led to increased insulin resistance. In the control group (without the characteristic symptoms of polycystic ovary syndrome), increased SFA intake and increased protein led to increased insulin resistance. Another finding of the present study was the effect of macronutrients such as a protein on insulin resistance. In the present study, high protein intake increased insulin resistance. Consistent with the present study is the study of ATTICA, which had a positive correlation between protein intake and insulin resistance [21]. One of the studies that are inconsistent with the present study is the He-Xia XIA study, which was performed to compare diet composition in women with and without PCOS. The 86 women (47 with PCOS and 39 without PCOS) participated in this study. The results showed a negative correlation between protein intake and HOMA-IR. Consequently, with increased protein intake, insulin resistance decreased [24]. Perhaps the reason for the difference with the present study is the difference in the number of research units. In the present study, 151 patients were in the PCOS women group and 31 women in the control group. Also in this study, subjects were homogeneous in terms of BMI.

Conclusion

In the present study, considering the relationship between some dietary components (increased calories, increased total fat intake, lower consumption of PUFA and MUFA unsaturated fats, increased consumption of SFA saturated fats, and high protein intake) and insulin resistance, it is important to study the dietary pattern and its modification in the management of people with PCOS. Even in the control group (without clinical or laboratory evidence of diagnosis of polycystic ovary syndrome), some nutritional factors (More SFA saturated fat intake and high protein intake) were associated with insulin resistance. Therefore, modifying the dietary pattern can

improve the status of PCOS and prevent the potential risks of insulin resistance (such as metabolic syndrome, T2DM and cardiovascular disease) in different PCOS subtypes. In general, the results of this study suggest balance in carbohydrate and fatty acids intake and dietary fiber intake to improve health parameters in PCOS patients. Also, the results of this study suggest several applications clinical trials based on the effects of dietary factors affecting insulin resistance and complementary studies to find differences in dietary patterns in different PCOS subtypes separately and determine the association of undesirable metabolic profiles with dietary components in each disease phenotype.

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Limitations

The limitations of this study include the lack of cooperation of many physicians in requesting appropriate tests. On the other hand, some research units did not perform the requested tests.

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References

1. Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, et al. Diagnosis and treatment of polycystic ovary syndrome: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013;98(12):4565-92.
2. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81(1):19-25.
3. Azziz R, Marin C, Hoq L, Badamgarav E, Song P. Health care-related economic burden of the polycystic ovary syndrome during the reproductive life span. J Clin Endocrinol Metab. 2005;90(8):4650-8.
4. Aali B, Naderi T. Evaluation of clinical, ultrasound and laboratory features of PCOS in Kerman in 1381. Iran J Endocrinol Metab. 2004;6(2):153-61.
5. Kauffman RP, Baker VM, Dimarino P, Gimpel T, Castracane VD. Polycystic ovarian syndrome and insulin resistance in white and Mexican American women: A comparison of two distinct populations. Am J Obstet Gynecol. 2002;187(5):1362-9.
6. Gabrielli L, Aquino EM. Polycystic ovary syndrome in Salvador, Brazil: A prevalence study in primary healthcare. Reprod Biol Endocrinol. 2012;22;10:96.
7. Ramezani FT, Rashidi H, Azizi F. The prevalence of idiopathic hirsutism and polycystic ovary syndrome in the Tehran Lipid and Glucose Study. Reprod Biol Endocrinol. 2011;9:144.
8. Moran LJ, Ranasinha S, Zoungas S, McNaughton SA, Brown WJ, Teede HJ. The contribution of diet, physical activity and sedentary behaviour to body mass index in women with and without polycystic ovary syndrome. Hum Reprod. 2013;28(8):2276-83.
9. Conway G, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Franks S, Gambineri A, et al. The polycystic ovary syndrome: A position statement from the European Society of Endocrinology. Eur J Endocrinol. 2014;171(4):1-29.
10. Berek NJ. Berek and Novaks gynecology. 15th ed. 2012.
11. Zangeneh F, Naghizadeh M, Bagheri M, Jafarabadi M. Are CRH & NGF as psychoneuroimmune regulators in women with polycystic ovary syndrome? Gynecol Endocrinol. 2017;33(3):227-33.
12. Hernández-Valencia M, Hernández-Rosas M, Zárate A. Care of insulin resistance in polycystic ovary syndrome. Ginecologia y obstetricia de Mexico. 2010;78(11):612-6.
13. Abu-Wasel B, Walsh C, Keough V, Molinari M. Pathophysiology, epidemiology, classification and treatment options for polycystic liver diseases. World J Gastroenterol. 2013;19(35):5775-86.
14. Ehsani B, Moslehi N, Mirmiran P. Effects of hypo-caloric D diet and dietary composition on reproductive and metabolic disorders in women with polycystic ovary syndrome: A review of studies. Iran J Nutr Sci Food Tech. 2015;10(2):103-14.
15. Blüher M. Adipose tissue dysfunction contributes to obesity related metabolic diseases. Best Pract Res Clin Endocrinol Metab. 2013;27(2):163-77.
16. Thomson R, Buckley J, Moran L, Noakes M, Clifton P, Norman R, et al. The effect of weight loss on anti-Müllerian hormone levels in overweight and obese women with polycystic ovary syndrome and reproductive impairment. Hum Reprod. 2009;24(8):1976-81.
17. Williams C. Macronutrients and performance. J Sports Sci. 1995;13(1):1-10.
18. Pehlivanov B, Orbetzova M. Characteristics of different phenotypes of polycystic ovary syndrome in a Bulgarian population. Gynecol Endocrinol. 2007;23(10):604-9.
19. Kasim-Karakas SE, Almario RU, Gregory L, Wong R, Todd H, Lasley BL. Metabolic and endocrine effects of a polyunsaturated fatty acid-rich diet in polycystic ovary syndrome. J Clin Endocrinol Metab. 2004;89(2):615-20.
20. Zivkovic AM, German JB, Sanyal AJ. Comparative review of diets for the metabolic syndrome: Implications for nonalcoholic fatty liver disease. Am J Clin Nutr. 2007;86(2):285-300.
21. Panagiotakos DB, Tzima N, Pitsavos C, Chrysohoou C, Papakonstantinou E, Zampelas A, et al. The relationship between dietary habits, blood glucose and insulin levels among people without cardiovascular disease and type 2 diabetes; the ATTICA study. Rev Diabet Stud. 2005;2(4):208-15.
22. Zhang J, Liu Y, Liu X, Xu L, Zhou L, Tang L, et al. High intake of energy and fat in Southwest Chinese women with PCOS: A population-based case-control study. PloS One. 2015;10(5):e0127094.
23. Sjaarda LA, Schisterman EF, Schliep KC, Plowden T, Zarek SM, Yeung E, et al. Dietary carbohydrate intake does not impact insulin resistance or androgens in healthy, eumenorrheic women. J Clin Endocrinol Metab. 2015;100(8):2979-86.
24. Stender S, Dyerberg J. Influence of trans fatty acids on health. Ann Nutr Metab. 2004;48(2):61-6.
25. He-xia XIA, Zhang W. Study of Association between Polycystic Ovary Syndrome and Dietary Intake. J Reprod Contracept. 2012;23(1):29-40.
26. Tehrani FR, Rashidi H, Khomami MB, Tohidi M, Azizi F. The prevalence of metabolic disorders in various phenotypes of polycystic ovary syndrome: a community based study in Southwest of Iran. Reprod Biol Endocrinol. 2014;12:89.
27. Hashemi S, Ramezani Tehrani F, Noroozzadeh M, Azizi F. Normal cut-off values for hyperandrogenaemia in Iranian women of reproductive age. Eur J Obstet Gynecol Reprod Biol. 2014;172:51-5.
28. Goodarzi MO, Dumesic DD, Chazenbalk G, Azziz R. Polycystic ovary syndrome: Etiology, pathogenesis and diagnosis. Nat Rev Endocrinol. 2011;7(4):219-31.
29. Schorge JO, Bradshaw KD, Halvorson LM, Schaffer JI, Corton MM.

Williams gynecology: McGraw-Hill Medical New York. 2008.

30. Kar S. Anthropometric C and metabolic comparisons of the four Rotterdam PCOS phenotypes: A prospective study of PCOS women. J Hum Reprod Sci. 2013;6(3):194-200.

31. Kim HM, Park J, Ryu SY, Kim J. The effect of menopause on the metabolic syndrome among Korean women: The Korean National Health and Nutrition Examination Survey, 2001. Diabetes Care. 2007;30(3):701-6.

32. Asghari G, Rezazadeh A, Hosseini-Esfahani F, Mehrabi Y, Mirmiran P, Azizi F. Reliability, comparative validity and stability of dietary patterns derived from an FFQ in the Tehran Lipid and Glucose Study. Br J Nutr. 2012;108(6):1109-17.

33. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. Public Health Nutr. 2010;13(5):654-62.

34. Hosseini-Esfahani F, Daneshpour MS, Mirmiran P, Mehrabi Y, Hedayati M, Azizi F. Interaction of APOC3 polymorphism and dietary fats on the risk of metabolic syndrome. Iran J Endocrinol Metab. 2015;16(5):345-55.

35. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28(7):412-9.

36. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004;27(6):1487-95.

37. Graff SK, Mario FM, Alves BC, Spritzer PM. Dietary glycemic index is associated with less favorable anthropometric and metabolic profiles in polycystic ovary syndrome women with different phenotypes. Fertil Steril. 2013;100(4):1081-8.

38. Douglas CC, Norris LE, Oster RA, Darnell BE, Azziz R, Gower BA. Difference in dietary intake between women with polycystic ovary syndrome and healthy controls. Fertil Steril. 2006;86(2):411-7.

39. Ebbeling CB, Leidig MM, Sinclair KB, Seger-Shippee LG, Feldman HA, Ludwig DS. Effects of an ad libitum low-glycemic load diet on cardiovascular disease risk factors in obese young adults. Am J Clin Nutr. 2005;81(5):976-82.

40. Brynes AE, Edwards CM, Ghatei MA, Dornhorst A, Morgan LM, Bloom SR, et al. A randomised four-intervention crossover study investigating the effect of carbohydrates on daytime profiles of insulin, glucose, non-esterified fatty acids and triacylglycerols in middle-aged men. Br J Nutr. 2003;89(2):207-18.

41. Homayounfar R, Ehrampoush E, Koohpaye SA, Meshkibaf MH, Taghizade S, Almasi A, et al. Diet-induced metabolic syndrome model in rats. J Fasa Univer Med Sci. 2013;2(4):288-96.

42. McLaughlin T, Craig C, Liu L-F, Perelman D, Allister C, Spielman D, et al. Adipose cell size and regional fat deposition as predictors of metabolic response to overfeeding in insulin-resistant and insulin-sensitive humans. Diabetes. 2016;65(5):1245-54.

43. Tierney AC, Roche HM. The potential role of olive oil-derived MUFA in insulin sensitivity. Mol Nutr Food Res. 2007;51(10):1235-48.

44. Saidpour A, Kimiagar M, Zahediasl S, Vafa M, Ghasemi A, Abadi A, et al. Effects of high-fat diets based on butter or soybean, olive or fish oil on insulin resistance and plasma des-acyl ghrelin in rats. Iran J Nutr Sci Food Tech. 2011;6(3):39-48.