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Polycystic Ovary Syndrome and a Possible Role of Diet-Results from a Case Control Study in Kashmiri Women

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Research Article

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Abstract

Background: Polycystic ovary syndrome (PCOS) management with dietary interventions targeting underlying pathogenesis of obesity and insulin resistance has been challenging for decades. Various studies so far have reported that weight loss improves ovulation, testosterone levels and insulin resistance in women but the optimal diet composition has not been evaluated in detail. Hence, the current study was undertaken with the aim to explore the role of diet in management etiology of PCOS Kashmiri women.

Materials and Methods: In this case-control observational study, we randomly selected 145 PCOS patients and 145 healthy age and BMI matched controls. Dietary history was taken in detail including intake of macronutrients (fats, protein and carbohydrates) assessed by food frequency questionnaires (FFQ). Anthropometric data including weight, height, waist circumference, hip circumference and blood pressure was recorded. Patients were evaluated in detail for hirsutism, menstrual irregularity, and clinical evidence of insulin resistance. Additionally, blood samples were also collected for evaluation of clinical parameters from all the participants in this study.

Results: PCOS patients had higher waist circumference, systolic blood pressure and clinical evidence of hyperandrogenism (Ferriman Gallwey Score ≥8) in comparison of controls. Complete dietary evaluation of both cases and controls revealed that though overall intake of calories was nonsignificantly higher in PCOS case, major difference was in the macronutrient composition. PCOS cases had significantly higher dietary fat intake as compared to controls

(90.38 ± 8.79 vs 67.98±1.92gm/day; p<0.001). However, carbohydrate and protein intake could not attain any statistically significant difference among two groups.

Conclusion: Our results showed that despite similar total calorie intake fat intake is higher among PCOS cases. Thus habitual dietary fat intake increases PCOS risk, whereas proteins and carbohydrates do not have significant effect. However, more studies with increased sample size are needed to better validate the effects of dietary carbohydrates, fats and proteins on PCOS.

Keywords: Diet; Protein; Fat; Insulin Resistance; Obesity; Polycystic Ovary Syndrome

Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder among women of reproductive age. Its key features are biochemical and clinical hyperandrogenism associated with reproductive morbidity, including menstrual dysfunction and infertility [1]. The incidence of PCOS has risen substantially, from 6-8% to 12-20% as per the result of the adoption of the Rotterdam criteria for diagnosis [2-5].

Visceral adiposity is common is women with PCOS. In PCOS there is a clustering of metabolic disorders, including dyslipidemia, hypertension, impaired glucose tolerance, and hyperuricemia. This has been collectively termed as Metabolic Syndrome or Syndrome X. Women with PCOS usually display one or more of the above mentioned metabolic derangements Insulin resistance is strongly implicated in the etiology of both metabolic syndrome and PCOS [6,7].

There is a strong evidence has been reported that it is the visceral fat compartment that correlates with insulin resistance and metabolic syndrome [8,9]. Women with visceral obesity have been found to have the highest peak of Cardiovascular diseases (CVDs), diabetic mortality and morbidity, insulin resistance, dyslipidemia, hypertension and left ventricular enlargement [10]. It has also been reported that women with PCOS have a tendency to accumulate abdominal fat, as defined by their waist hip ratio (WHR) [11]. Studies have shown that adipose tissue has effects even on eating behavior, energy expenditure and body weight [12,13]. Central obesity leads to decreased secretion of adipocyte-derived peptide hormones like adiponectin- a major adipocytokine that is considered to play positive role in decreasing insulin resistance [14].

Total fat and monounsaturated fat intakes are positively associated with plasma leptin concentrations even after adjusting for BMI and other confounding factors [15].

However there is scant data regarding the influence of specific dietary factors on circulating leptin concentrations among PCOS women. However, reduction of 24-hour circulating leptin concentrations in women by the consumption of high-fat meals has been reported in few studies [16]. A study has reported negative association of leptin with energy intake from carbohydrates and a positive association with energy from dietary fat in healthy subjects [17].

Gherlin levels have been associated with insulin resistance and positive energy balance or obesity [18-25]. Studies on the effect of various dietary factors on PCOS patients in our Kashmiri population are sparse. Thus, this study was conducted with an aim to examine the relationship between habitual dietary components (proteins, fats and carbohydrates) in PCOS women as compared to healthy controls.

Materials and Methods

Study Participants and Data Collection

In this study we enrolled 145 PCOS patients and 145 healthy age and BMI matched controls at Sher-i Kashmir Institute of Medical Sciences Srinagar (SKIMS) from Feb 2018 to Jan 2019. The study participants were selected from an outpatient setting in the Department of Gynecology and Obstetrics, SKIMS. All the participants were recruited after signing informed consent approved by the local Institutional review board. Diagnosis of PCOS was made using Rotterdam criteria [2]. The Ethics Committee of SKIMS approved the study protocol. Medical history, physical examination and complete blood profiling determined health status of the control group. Control group participants had no signs or symptoms of

PCOS, which included health staff, attendants and patients who presents with different symptoms. Exclusion criteria for all subjects included pregnancy, hypothyroidism, hyperprolactinemia, congenital adrenal hyperplasia (CAH), current or previous (within the last 3 months) use of oral contraceptives, glucocorticoids, anti-androgens, ovulation induction agents, anti-diabetic and anti-obesity drugs or other hormonal drugs.

In each subject we measured height and weight to calculate Body Mass Index (BMI). Body height was measured to the nearest 0.1 cm by an electronic scale (Prestige, India) with the subject standing without shoes. Body weight was measured in light indoor clothing to the nearest 0.1 kg by an electronic scale (Dr. Moorpen's, India Ltd). The BMI was calculated using the standard formula of weight (kg)/height (m^2). Waist circumferences were measured by inch tape at the level of umbilicus. Blood pressure (BP) was measured up to 1mm using a standard mercury BP apparatus (Diamond, India). Furthermore, a brief clinical examination was done to rule out any overt medical condition such as syndromic presentations, short stature, features of rickets and disorders of sexual differentiation (DSD).

Dietary Intake

Dietary intake and habits were assessed using food frequency (FFQ) questionnaires. Participants were asked to recall the type and amount of food and beverage consumed using standard household measures (cups, tablespoons, etc.). Food intake data obtained from the PCOS and healthy control groups were analyzed for carbohydrates, proteins and fats.

Biochemical Assays

After undergoing required checkup including physical examination, medical history as well as dietary data collection, venous blood sampling was taken for the biochemistry and hormonal assays including testosterone, LH, FSH, prolactin and 17(OH) Progesterone. A fasting blood sample at 8:00-9:00 hours after a 12-hour overnight fast was obtained from each subject for biochemical and hormonal estimation. The biochemical parameters were assayed using fully automated analyzerC311, Hitachi Japan and hormones by electrochemiluminiscence (Cobas E 411, Hitachi Japan). The analyses were carried out during the early follicular phase in women who had menstrual cycles and in any phase of the cycle in PCOS patients.

Statistical Analyses

Results are expressed as mean ±SD. Comparisons between two groups were made using the independent samples t-test. Pearson's correlation analyses were performed to define correlations between parameters. Statistical evaluations were performed by running the STATA software, version 12 (Stata Corp., College Station, TX, USA). P values of less than 0.05 were regarded as statistically significant.

Results

A total of 290 subjects were included in this observation study. Among them 145 were PCOS cases and 145were age and BMI matched controls. The data regarding different clinical parameters assessed in both groups is given in Table 1. Among various anthropometric parameters assessed PCOS cases had significantly higher waist circumference than controls (83.89+ 1.34 vs 74.51+1.20; p<0.01). Among clinical parameters PCOS cases were found to have significantly higher systolic blood pressure than controls. PCOS cases were found to have significantly higher Ferriman gallaway score (13.77+1.35 vs 6.55+0.36); p<0.01 (Table 1). On restricting the analysis to different dietary components, dietary carbohydrate and protein consumption was almost similar in both groups (p> 0.05). However, the dietary fat intake was significantly higher among PCOS cases than control subjects was statistically significant (90.38 + 8.79 vs 67.98+1.92); p <0.001(Table 2).

Variable	Cases (n=104) Mean ± SD	Controls (n=45) Mean ± SD	P value
Mean Age(years)	23.75±0.51)	24.44±0.76	0.456
Menarche age(years)	12.96± 0.14	12.2±0.14	0.0023
Weight (kgs)	61.29 ±1.49	60.49±1.92	0.740
Height (cms)	155.38±0.55	151.11±0.88	<0.01
BMI(kg/m^2)	25.66±0.65	26.81±0.77	0.260
Waist (cms)	83.89± 1.34	74.51±1.20	<0.01
Hip (cms)	91.32±0.76	88.04±0.83	0.066
Systolic blood pressure (mm Hg)	119.60 ± 1.11	112.85±2.85	0.039

Diastolic blood pressure (mm hg)	79.65 ± 0.78	77.14±1.84	0.266
Ferriman score	13.77±1.35	6.55±0.36	<0.01

Kg:kilogram; cm:centimetre; kg/m2:kilogram per meter square; mm Hg: millimeter of mercury

Table 1: Clinical Characteristics of PCOS cases and controls.

Variable	Cases (n=104) Mean ± SD	Controls (n=45) Mean ± SD	P value
Serum Total Cholesterol (mg/dl)	210.81+42.92	177.14+38.96	0.53
Plasma glucose post OGTT 1hour (mg/dl)	142.25+7.53	134.10+4.26	0.407
Plasma glucose post OGTT 2hour (mg/dl)	120.12+4.32	115.16+4.92	0.58
Bilirubin(mg/dl)	0.99+0.07	0.86+0.07	0.291
Albumin(g/dl)	4.74+0.22	4.58 + 0.07	0.748
Kcal /day	2119.13+51.31	2053.03+85.10	0.491
Carbohydrates(gms)/day	312.54+11.38	277.95+14.65	0.08
Protein (gms)/day	60.46 +1.75	58.73+3.02	0.603
Fat (gms)day	90.38+8.79	67.98+1.92	<0.001

Table 2: Dietary and biochemical parameters of PCOS case and controls.

Discussion

Obesity and insulin resistance are considered as one of the essential components in the pathogenesis of PCOS thus highlighting the importance of observing the effect of diet on PCOS. Marsh, et al. [26] were first to provide objective evidence to justify the use of low-GI (glycemic index) diets in the management of PCOS in women.

In the present study we assessed the dietary patterns of PCOS and compared it with age and BMI matched healthy controls, to elicit the metabolic importance of dietary nutrients in PCOS. The results indicated a significant association of habitual dietary fat in PCOS patients. Mavropoulos, et al. (2005) have reported that adherence to low carbohydrate, ketogenic diet led to improvement in body weight, free testosterone, LH/FSH ratio, fasting serum insulin and symptoms in women diagnosed with PCOS [27]. Another study has shown that low carbohydrate diet has a minor additional effect to calorie restriction in terms of weight loss when compared to a standard diet [28].

Kong, et al. [29] examined the cross-sectional associations of ghrelin and leptin with the habitual macronutrient intake of 165 healthy overweight and obese sedentary women and tested the modifying role of insulin in these associations. Diets higher in fat and carbohydrate are associated with a hormonal profile (i.e., lower leptin and higher ghrelin concentrations), which could enhance weight gain, particularly among individuals with higher circulating insulin concentrations [29]. One more study by Douglas, et al. [30] have shown that reduction in dietary carbohydrate reduces the fasting and post-challenge insulin concentrations in women suffering from PCOS which overtime may prove beneficial to PCOS women as far as endocrine and reproductive variables are concerned.

In contrast to these studies, other studies failed to show any association between dietary fat and its subtypes with PCOS [15,16,31-33]. However, these studies were all conducted in healthy subjects or in other non-PCOS patients.

One study on dietary intake of PUFA (polyunsaturated fatty acids) has revealed that increased dietary PUFA intake can exert significant metabolic and endocrine effects in women with PCOS. It was demonstrated in this study that PUFA intake alters glucose homeostasis, plasma lipids and sex steroids in PCOS women [34].

Androgen excess plays an important role in the development of PCOS [35]. Number of studies has shown the role of fat and fatty acids in androgen synthesis [14,36-38]. Present study found no significant difference in carbohydrate consumption in PCOS and controls. However, Mavropoulos, et al. found that low carbohydrate diet to some extent can benefit women with PCOS [27]. Barber, et al. [39] showed that ghrelin levels were suppressed by oral glucose in women with PCOS. Moran, et al. [40] in their studies have concluded that the postprandial ghrelin response is impaired in obesity and that weight loss increases fasting ghrelin levels. Some

studies have reported that in PCOS women protein intake suppressed glucose consumption [14].

It is generally accepted that carbohydrate is the most effective macronutrient for rapid absorption and has greater insulin secreting effect, whereas proteins induce a prolonged effect and fat exhibits weak capacity [41]. Sorenson, et al. [42] have found that the replacement of carbohydrates with protein in ad libitum diets improved weight loss as well as glucose metabolism, thus it seems to provide an improved dietary treatment for PCOS women.

Our study results show that despite comparable intake of total calories in PCOS cases to controls higher fat intake in PCOS is a major dietary macronutrient responsible for metabolic imbalance that needs to be modified during dietary counseling of PCOS cases [43,44].

Our study had some limitations. Use of self-reported dietary intake without any unit measurements, may results the potential for recall bias and under reporting. In addition, the sample size of our study is too less to authenticate our findings.

Conclusion

The results of the current study showed diet rich in fat could be the important dietary components in the development of PCOS. The increasing short-term dietary intervention studies have coherently shown that weight loss with dietary modifications can normalize reproductive and endocrine parameters of PCOS women. Current conservative treatment should emphasize sustainable weight loss through dietary fat restriction and exercise. The need of the hour is that lifestyle modification should be made priority in management of PCOS wherein dietary intervention can play a key role.

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