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Challenges and opportunities**

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# **Nutritional Management in Polycystic Ovary Syndrome: Challenges and opportunities**

### *Abstract*

PCOS is one of the most common endocrine diseases affecting women of reproductive age. Its etiology remains unresolved but it is thought to have a genetic basis as well as interactions with other environmental factors. This disease is diagnosed through the Rotterdam 2003 criteria but there is no definite treatment for the disorder. However, cure involves targeting the multiple symptoms of PCOS where weight loss is the first-line intervention. Obesity may not be the universal feature of PCOS, but studies have shown that there is a high prevalence among diseased females. Since the patients are more likely to be obese, they are also more likely to develop insulin resistance. The proper diet for PCOS thus targets these two characteristics of the disorder and through their management, the other symptoms of PCOS including hirsutism, acne and infertility are targeted. Saturated fats consumption should be reduced to a minimum whereas the unsaturated fat intake must be balanced with the carbohydrate and protein intake. Carbohydrate intake should not be abundant in the diet because high GI foods prove to reduce insulin sensitivity and increase the risk of type 2 diabetes. As for the protein intake, it should not exceed 20% of the total macronutrient calorie intake. A healthy lifestyle must be followed which includes at least 30 minutes of exercise, five times a week. A properly managed diet combined with a balanced lifestyle addresses insulin resistance, cardiovascular health and metabolism, all of which target PCOS symptoms and alleviate them.

**Keywords:** PCOS, fats, carbohydrates, proteins, insulin resistance, diabetes, hirsutism, infertility, , glycaemia, glycemic index, physical activity, lifestyle, diet

## *Introduction*

Polycystic ovary syndrome (PCOS) is the most common endocrine disease affecting 10% of reproductive age women (Pfeifer et al, 2009;Jeans et al, 2009). It is considered a heterogeneous disorder, generally characterized by a triad of oligomenorrhea, hirsutism, and obesity. PCOS may involve further complications including type 2 diabetes, increased risk of metabolic syndrome, and a possibility of cardiovascular disease and endometrial cancer. It is also considered the leading cause of infertility in women.

The etiology of PCOS still remains unresolved although it is known to have a strong association with hyperandrogenism. It has been shown, however, that PCOS may have a genetic basis. That is, there have been reports proving the increased prevalence of PCOS in first-degree relatives of affected women (Kandarakis et al, 2005). Studies of relatives of patients suffering from PCOS show that 24% of mothers and 32% of sisters are affected, supporting the association between PCOS and genetic factors (Pfeifer et al, 2009). Specific genes responsible for this disease are not known, but candidate genes are proposed. In addition to this, there are also some non- heritable factors that are thought to contribute to the phenotypic manifestation of PCOS. The disorder is considered to manifest due to several inborn genetic traits that interact with other innate or environmental factors. This eventually results in deregulation of steroidogenesis (Ehrmann et al, 1995). In addition to this, there may be differences within populations and ethnic groups that show a higher risk of PCOS. In a study comparing the prevalence of PCOS between African-American and Caucasian American women, African-American women were almost twice as likely to develop PCOS than the white with 8% and 4.8 % respectively (Norman et al, 2004).

As for PCOS diagnosis, there are several proposed diagnosis criteria but there is not a single test that identifies the disorder. Nevertheless, there is worldwide agreement to label a woman PCOS positive or negative. The disorder is diagnosed if at least two of the following conditions are present:

1. Oligovulation and/or anovulation
2. Clinical and/or biochemical signs of hyperandrogenism
3. Polycystic ovaries identified by ultrasound

These are known as the Rotterdam 2003 criteria and remain viable until the present day.

Women with PCOS experience a number of abnormalities that demand consideration including oligomenorrhea, hyperandrogenism, infertility, and metabolic risk factors such as obesity and insulin resistance. However, there is no definite treatment for the syndrome as a whole. Cure involves targeting the multiple medical conditions arising from PCOS to ameliorate the overall symptoms (Moran et al, 2009). A multidisciplinary approach is needed in the treatment of the patient suffering from PCOS. The first-line intervention for women includes weight loss in order to recover proper ovulation and reduce metabolic risk factors. Studies show that even a small percent reduction in body weight, as small as 5 to 10 percent, may restore normal ovulation and increase the probability of pregnancy (Crosignani, 2003). Weight loss also decreases serum androgen levels, which may lead to improvements in hirsutism (Moran, 2011). This further supports the importance of a balanced diet, healthy lifestyle and weight loss. No one diet has been proven superior to another. This paper will discuss the findings of studies concerning modifications in eating habits (diet, nutrition) and propose some nutritional solutions that contribute to lifestyle-modification approach to PCOS. The relationship between PCOS, obesity and insulin resistance will be discussed, then follows a discussion of the effects of specific dietary management in PCOS.

### *PCOS and Obesity*

Although a controlled systematic study has not been yet performed to determine the prevalence of PCOS with obesity in women, studies have shown that 70% of women with PCOS are obese (Douglas et al, 2006). Despite the aforementioned, obesity can generate many complications, one of which could be linked to PCOS. Obesity results in complex interactions between the pancreas, pituitary gland and ovary, resulting in alterations in the normal hormonal secretion patterns. Accordingly, there are significant effects on menstrual or ovulatory disturbances in PCOS, and these are pronounced in the obese. Obesity also results in higher androgen levels, contributing to hirsutism and acanthosis nigricans.

Although obesity is not a universal feature of PCOS, several studies report prevalence of obesity ranging from 42% in an unselected Southeastern population to approximately 70% in a referral population (Carmina 2006). An unselected Spanish population of women with PCOS reported a 30% rate of obesity. Another Greek survey of women with PCOS reported a 38% rate (Gambineri 2002). This percentage differs among populations and ethnic groups. The variation is due to genetic

factors, nutritional intake, and lifestyle. Cultural differences may alter the effects of PCOS. In the United Kingdom, for example, approximately 33% of women with PCOS are obese (Jeans et al, 2009), while in the United States, nearly 70% of women with PCOS are obese (Douglas et al, 2006). Thus, treatment of obesity in the management of PCOS will continue to play a major role.

Women with PCOS who are overweight or obese showed a greater abdominal or visceral adiposity compared with weight-matched controls (Moran et al, 2009), this further worsening insulin resistance. Epidemiological studies suggest an association between saturated fat intake and reduced insulin sensitivity. Abdominal fat has a strong association with insulin resistance, hyperandrogenism, and PCOS. Indeed, Huber-Buchholz et al found that abdominal fat loss was correlated with the restoration of ovulation (Moran et al, 2002). A reduction of as little as 5% of the total body weight reduces insulin and testosterone levels, and improves menstrual function and symptoms of hirsutism and acne (Kate et al, 2005).

There exists a strong correlation between the hormone leptin and obesity, hence being frequently associated with PCOS (Norman et al, 2004). Solely the adipose cells produce this hormone, which helps regulate energy balance by inhibiting hunger. Insulin resistance and hyperinsulinemia, both characteristics of PCOS, are seen to be linked to leptin and its receptors. The results of a study carried out by Dr. Chakrabarti provide evidence that hyperleptinemia in PCOS women appears to be due to the positive correlation between serum leptin, BMI, and insulin (Chakrabarti, 2013). However, other studies have shown that there is no difference in leptin in PCOS compared to healthy subjects (Houjehani et al, 2012). One other hormone affecting obesity, also associated with PCOS, is ghrelin. Ghrelin opposed the actions of leptin by inducing hunger. This protein hormone is made up of 28 amino acid. It is an acylated peptide produced primarily by the stomach's endocrine cells and secreted into the circulation (Norman et al, 2004). Before meals, secretion of ghrelin stimulates feeding, decreases energy expenditure, and stimulates gastric motility and acid secretion. There are conflicting studies for the relation on ghrelin levels in PCOS patients, where some show low levels of ghrelin in PCOS, while others show increased levels (Houjehani et al, 2012).

One of the proposed mechanisms for the increased risk of endometrial carcinoma in patients with PCOS may be related to higher levels of androgen (male hormones) and estrogen levels and lower levels of progesterone. The resulting hormone imbalances can stimulate the endometrium and even lead to endometrial cancer (Norman et al, 2004).

### *PCOS and Insulin Resistance*

As noted previously, PCOS patients who are obese are more likely to develop insulin resistance, than those who have normal body weight (Normal et al, 2004). This is due to the adipose tissue of obese patients, which secretes free fatty acids and tumor necrosis factor- $\alpha$ , both of which contribute to the development of insulin resistance (Salehi et al, 2004). However, insulin resistance is observed in PCOS subjects independent of their body mass and rates of glucose intolerance are 5 to 10 fold higher than normal (Moran et al, 2009). Women with a first degree relative with type 2 diabetes are particularly prone to acquire the syndrome.

In PCOS, compensatory hyperinsulinemia results in pleiotropic effects including co-gonadotrophic stimulation of ovarian and adrenal steroidogenesis. In type 2 diabetes, insulin resistance contributes towards  $\beta$ -cell exhaustion and ultimately to hyposecretion of insulin with resultant dysglycemia. The link between PCOS and Type 1 diabetes mellitus is believed to implicate supraphysiological concentrations of insulin within the systemic circulation (Barber 2012).

### *The Right Diet for PCOS*

Weight loss strategies in PCOS include calorie-restricted diets and physical exercise, targeting obesity and insulin resistance, both of which are characteristics of PCOS patients.

At the beginning, nutritional intake can be modified to focus on a general reduction of weight which can itself ameliorate acne and hirsutism, as well as boost fertility in patients seeking to become pregnant. In the long run, the dietary management attempts to decrease the risks of type 2 diabetes, cardiovascular diseases and certain types of cancer (Kate et al, 2005). Thus, the appropriate diet will address the multiple conditions of PCOS, alleviating the symptoms of the disease as a whole. The diet involves managing both the calorie intake, which ought be carefully determined, as well as the nutrient biomolecule consumption. Fats, carbohydrates and proteins, each have their essential role in the human metabolism, and thus their appropriate intake should be accounted for when considering the right diet for PCOS patients.

The standard caloric intake for women lies between 1600 and 2000 calories per day. This varies according to body mass, physical activity and age. Dieting requires either reducing the macronutrient intake or elevating physical activity, or both. Combining the two methods into one

regime provides the optimum results. However the initial step of dietary management should focus on the macronutrient composition of the diet and the eating pattern, before targeting accelerated weight loss (Moran et al, 2009). The purpose of this is to reduce abdominal fat and improve insulin sensitivity (Moran et al, 2006). Additionally, patients who exercise have lower body fat and increased lean body tissue, resulting in increased resting energetic expenditure. This improves the metabolism of women with PCOS whose ultimate goal is an ideal body weight and composition.

### ***The effect of fats in the PCOS diet***

Fat is a macronutrient whose metabolism releases more the double the energy released by carbohydrate metabolism: nine kilocalories per gram and four kilocalories per gram respectively. However, excess carbohydrate intake or its incomplete oxidation results in its conversion to fats through lipogenesis. In addition, the consumption of trans fats leads to heightened risk of ovulatory infertility and increased insulin resistance linked to type 2 diabetes (Chavarro et al, 2007). Excess body weight is also associated with higher risk of cardiovascular diseases.

The fat tissue in PCOS patients produces inadequate amounts of the hormone that regulates fat and glucose processing, leading to increased insulin resistance, higher risks of diabetes and heart diseases (Chazenbalk et al, 2010). Therefore, weight loss strategies should include reduction in fat intake, especially trans fats, to target the aforementioned symptoms in PCOS. Moderate consumption of unsaturated fatty acids has shown to improve insulin sensitivity in diabetic and obese individuals. Furthermore, several studies have shown positive results with diets that include polyunsaturated fatty acids (PUFA). Eicosapentaenoic acid and docosahexaenoic acid are long chained PUFA present mainly in fish oil, which have positive effects on all patients (McAuley et al, 2005). These include improving blood cholesterol levels, decreasing the risks of heart diseases. PUFAs can also decrease the risk of type 2 diabetes, further being used to produce Omega-3 which itself protects the heart and reduces blood pressure.

Overall, dietary fat should account for no more than 30% of the calorie content of the diet, with a maximum of 10% of calories coming from saturated fat. The remainder of the fat content should be a balanced mixture of unsaturated fat including cooking oils and spreads (Norman et al, 2004).

### ***Carbohydrates as a macronutrient in the PCOS diet***

The glycemic load of food is the amount of carbohydrates taken multiplied by the glycemic index (GI). Increased glycemic load is caused by high GI food, which delivers carbohydrates after ingestion and increases the risk for type 2 diabetes (Miller, 2005). It was shown that intake of low GI foods is linked to enhanced insulin sensitivity and reduced postprandial hyperglycemia, increasing HDL and decreasing triglyceride levels of the blood. In addition, low GI foods have shown to protect against developing diabetes. Glycemic load can be reduced by following an isocaloric diet, which refers to substituting carbohydrates with monounsaturated fatty acids (MUFA) or protein, or by replacing high GI foods with lower GI food. Much scientific attention have been given to low carbohydrate diets which are also able to improve cardio-metabolic profile, reducing the risk of coronary heart disease (Kennedy et al, 2005). By following a low carbohydrate diet for 6 months, patients at risk of type 2 diabetes can achieve significant weight loss (Samaha et al, 2003). Thus, a low-GI diet, aids insulin resistance and benefits women with PCOS (Kate et al, 2005).

Several studies have been carried out, including both high-carbohydrate diets and low-carbohydrate diets. The results of these showed no significant differences on fasting insulin and insulin sensitivity (Dansinger et al, 2005). However, in low-carbohydrates subjects, a lower postprandial insulin response and improvements in triglycerides and HDL cholesterol were reported, as stated earlier with respect to the low GI foods (Stamets et al, 2004). Moreover, in some clinical trials, restricted carbohydrate diets have shown to improve adipokine levels and insulin sensitivity alongside reduced risks of cardiovascular problems (Fransworth et al, 2003). Nevertheless, in the long term, low-carbohydrate diets were associated with harmful effects on the lipid profile and should therefore be used only for a short period of time to ensure weight loss. (Moran et al, 2003).

### ***The benefits of protein intake in the PCOS diet***

As for the amount of protein in the diet, it is known that greater quantities increase satiety and postprandial thermogenesis, lowering the abdominal fat (Paddon et al, 2008). Recent studies have proven that a high intake of protein leads to improved glucose and insulin response to glucose load. Another study compared high-protein-low-carbohydrate diet (over a 1 month period) with low-protein-high-carbohydrate diet (over a 3 month period). The results showed no convincing differences between low and high protein content in terms of weight loss (Brehm et al, 2003). Yet an additional study showed that a high protein diet resulted in minor differential improvements for high-density lipoprotein (HDL-C, TC/HDL-C), AUC for glucose, and Femoro-Acetabular

Impingement (FAI) (Moran et al, 2003). Nonetheless, protein intake is essential to protect lean body tissue, which can improve the metabolism of PCOS patients. Ergo, 20% of a diet's calories should be protein (Samaha et al, 2003).

### ***Glycaemia with relation to eating habits in PCOS patients***

Blood glucose concentration (glycaemia) plays a role in regulating appetite and thus increasing caloric intake. Insulin and glucose fluctuations are widely seen in insulin resistant subjects and increase reactive hypoglycemia (Brinkworth et al, 2004). In a study on 64 lean PCOS women, 50% showed reactive hypoglycemia after a glucose load (Altuntas et al 2005). It occurred in women with increased Beta cell function and was associated with low androgen and prolactin levels (Samaha et al, 2003). Most PCOS women report phases of carbohydrate cravings, delaying the process of weight loss (Cardillo et al, 2003). Thus, hypoglycemia occurs in PCOS patients, which stimulates their eating behaviors and leads to a higher calorie and fat intake. This higher intake is due to the fluctuations in blood glucose in PCOS women and leads to alterations in body composition (Nordmann et al, 2006).

### ***Fertility and diet in PCOS***

There are few studies on the effect of dietary composition on fertility in women with PCOS. It was shown that there is no difference in menstrual cycles when a high-protein or a low-protein diet was followed (Moran et al, 2003). One study, however, suggested that a PUFA-rich diet can significantly increase urinary pregnanediol 3-glucuronide in PCOS women. In this study only two of seventeen subjects showed signs of ovulation. Luteinising hormone (LH), follicle-stimulating hormone (FSH), dehydroepiandrosterone sulfate, sex hormone-binding globulin, and testosterone levels showed no changes (Kasim-Karakas et al, 2004). Another study showed that caloric restriction causes reproductive function improvements regardless of weight loss (Moran et al, 2003)

### ***Physical Activity as a treatment for the symptoms of PCOS***

Due to the limited number of studies regarding physical activity in PCOS patients, recommendations are derived from studies on non-PCOS subjects. A general healthy lifestyle includes 30 minutes of exercise at least five days per week, where high intensity exercise (60-75 minutes) has a significant effect on weight loss. Several types of physical activity including aerobics,

endurance and resistance training, increase fitness and energy expenditure. Resistance training also increases muscle mass and thus resting energy expenditure, consequently influencing insulin sensitivity and enhancing metabolism (Jakcic et al, 2003).

### *Lifestyle Modification*

Women with PCOS were observed to have low self esteem combined with depression, and distorted self-image. Therefore, lifestyle intervention is necessary.

These modifications include weight loss, decreased trans-fat intake and increased physical activity, all of which show positive results in women with PCOS. Weight loss of 5%-10% of initial body weight, has also improved ovulation and fertility in women (Crosignani et al. 2003; Moran et al, 2003). In addition, there appears to be a high prevalence of smokers among PCOS. In one study, up to 50% of the women presenting to a clinic in Adelaide were current smokers (Norman et al, 2002). Hence, the proposal to quit smoking is also another important lifestyle factor to address. Several steps can be followed to ensure an improved lifestyle for women with PCOS, allowing them improved outcomes in the future.

1. Start with a daily energy requirement of 2000 to 2400 Kcal for sedentary subjects.
2. Exercise on a regular basis for at least 30 min daily, five time per week to maintain body weight. To provoke weight loss, prolonged and vigorous exercise is recommended.
3. Restrict saturated fat to less than 10% and make sure that the daily calorie intake of fat is around 30%.
4. Restrict refined carbohydrate and maximize high fiber and wholegrain carbohydrates. Remember that carbohydrate intake should range between 45-55%.
5. Use lean sources of protein rather than fatty sources. Keep in mind that daily protein intake should be around 20%, of total caloric intake. Satiety and insulin sensitivity is improved by this protein component of the diet.
6. Eat fish twice a week with at least one being an oily fish to obtain long-chain fatty acids (Omega-3).
7. Distribute fruits and vegetables in five portions a day in order to promote satiety and fiber supply.

- 8.** Eat three main meals per day with two healthy snacks, and do not skip a breakfast meal.
- 9.** Refrain from high caloric food and snacks that cause hyperinsulinemia and provoke hunger. Count drinks (fresh juice and alcoholic drinks) in the daily calorie allowance.
- 10.** Remember that weight loss causes health benefits. This can be achieved by restricting by 200 calories. A 500 kcal restriction per day leads to a 0.5 kg loss of weight per week.

### *Conclusion*

Despite the fact that there is no definite cure for PCOS, targeting the symptoms of the syndrome help to alleviate it. Thus, with a properly managed diet combined with a balanced lifestyle, insulin resistance, cardiovascular health and metabolism can be addressed. Further studies will allow discovery of the best diet and lifestyle to ensure optimal weight loss and reduce insulin sensitivity, leading to improved management of PCOS.

	Fat	Carbohydrate	Protein
Negative impact on pcos	(Saturated fatty acids and trans fats) -Ovulatory infertility -Insulin resistance -Type 2 diabetes -Heart diseases	(High GI foods) -increased risk of type 2 diabetes	Brehm's study comparing high-protein-low-carbohydrate diet with low-protein-high-carbohydrate diet showed no convincing differences between low and high protein content in terms of weight loss
Positive impact on pcos	(Unsaturated fats) -Improved insulin sensitivity -Decreased risk of heart disease -Improved blood cholesterol and pressure levels	(Low GI foods) -improved insulin sensitivity -postprandial hyperglycemia -increases HDL, decreases triglyceride level of the blood	-increases satiety -increases postprandial thermogenesis -lowers abdominal fat -protect lean body tissue, essential for PCOS metabolism
Quantity to be consumed in PCOS	-Saturated- $\leq 10\%$ of daily caloric intake -Unsaturated $\leq 20\%$ of daily caloric intake	-The two studies by Dasinger and Stamets-agree that a low carbohydrate diet should be followed -Study by Moran et al says that the low GI diet should be used for a short time - in the long-term : harmful to lipid profile	-20% of caloric daily intake
Comments	Intake includes cooking oil and spreads	PCOS patients are predisposed to Higher calorie intake due to hypoglycemia	Moran et al (2003) study shows that high protein diet resulted in minor differential improvements for high-density lipoprotein (HDL-C, TC/HDL-C), AUC for glucose, and Femoro-Acetabular Impingement (FAI

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