A Review on the Assessment of the Efficacy of the Diet in Women with Polycystic Ovary Disorder

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ABSTRACT
The polycystic ovary syndrome (PCOS) is defined as a combination of Hyperandrogenism (hirsutism and acne) and anovulation (oligomenorrhea, infertility, and dysfunctional uterine bleeding), with or without the presence of polycystic ovaries on ultrasound. It represents the main endocrine disorder in the reproductive age, affecting 6% - 15% of women in menacme. It is the most common cause of infertility due to anovulation, and the main source of female infertility. PCOS is becoming commoner due to increased awareness and the global increase in the prevalence of overweight and obesity. When in the presence of a menstrual disorder, the diagnosis of PCOS is reached in 30% - 40% of patients with primary or secondary amenorrhea and in 80% of patients with oligomenorrhea. PCOS should be diagnosed and treated early in adolescence due to reproductive, metabolic and oncological complications which may be associated with it. Treatment options include drugs, diet and lifestyle improvement. The optimal approach to dietary management of patients with PCOS gives beneficiary effects. Some studies revealed that PCOS is associated with overweight or obesity; successful weight reduction is the most effective method of restoring normal ovulation and menstruation. Low-carbohydrate diet and sustained regular exercise may help. It has been recommended that a diet in which a significant part of total carbohydrates is obtained from fruit, vegetables and whole grain sources may be helpful.

Keywords: Polycystic Ovary Syndrome, Infertility, Anovulation, Hyperandrogenism, Insulin Resistance.

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INTRODUCTION

The most common endocrine disorder, PCOS is becoming commoner due to increased awareness and the global increase in the prevalence of overweight and obesity. It is a heterogeneous disorder that has been difficult to define because there is no single abnormality or diagnostic test that defines the syndrome. While precise definitions are important for scientific studies, as a working definition the syndrome may be diagnosed if at least two of the following are present:

• Oligomennorhoea or amenorrhoea associated with decreased ovulation. PCOS is the commonest cause of anovulatory infertility.

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

• Abnormal ovarian ultrasound with 12 or more follicles in each ovary each having a diameter of 2-9mm, or increased ovarian volume.

• Increased LH with increased LH/FSH ratio. The diagnosis is more certain with the presence of increasing number of features. Many overweight or obese women have menstrual irregularity, decreased fertility or hirsutism without fulfilling diagnostic criteria for PCOS.

The pathogenesis and management of these is the same as for women with PCOS. Specific treatments for hirsutism and subfertility have substantially improved management of PCOS in recent years but do not generally influence the underlying condition which is largely due to over-nutrition and insulin resistance. Even PCOS patients who are not overweight are often insulin resistant, and modest weight loss improves outlook in patients of near normal body weight. The association of PCOS with the abnormalities of metabolic syndrome (central obesity, dyslipidaemia, hypertension and glucose intolerance) is responsible for the documented relationship with type 2 diabetes, cardiovascular disease and hormonally-responsive cancers in later life[1,2]. This article reviews our understanding of nutritional aspects of PCOS, and proposes an approach to diet management and nutritional therapy in patients with PCOS. The optimal approach to dietary management of patients with PCOS remains to be defined[3].

Classification

PCOS affects women of childbearing age without higher prevalence by ethnic groups, but the signs and symptoms may differ by ethnicity. Today, the most widely used tool for diagnosing PCOS are still the “Rotterdam Criteria”; its prevalence is up to five times higher than when defined by the NIH criteria[4].
Only a third of patients have the classic form of the syndrome described by Stein and Leventhal in 1935. The concept of PCOS is very broad; it is clinically characterized by the presence of menstrual dysfunction, chronic anovulation and hyperandrogenism [5]. The three main consensuses on PCOS defined the criteria for diagnosis which are highlighted below:

**The Rotterdam ESHRE/ASRM—Sponsored PCOS Consensus Workshop Group Fertility and Sterility (2003)**
Presence of 2 out of 3 criteria:
1) Oligoovulation or anovulation;
2) Clinical or biochemical signs of hyperandrogenism;
3) Polycystic ovaries on ultrasound. As defined by the Rotterdam Criteria in 2003, polycystic ovaries have as their concept, the presence of at least one ovary of 12 or more follicles with diameters of 2 - 9 mm and/or increase the ovarian size > 10 ml (The ESHRE Rotterdam/ASRM, 2004). In addition to these criteria, other medical conditions that can cause chronic anovulation and androgen excess should be excluded, such as:
   - Hyperprolactinemia/hyperthyroidism;
   - Congenital adrenal hyperplasia, classical and nonclassical form;
   - Cushing’s syndrome; secretory ovarian tumor of adrenal androgens [4]

**The Thessaloniki ESHRE/ASRM—Sponsored PCOS (2006)**
In 2006, The Androgen Excess and PCOS Society (AE-PCOS) published its positioning regarding the diagnosis of polycystic ovary syndrome. According to this association, the androgen excess needs to be present, either by clinical signs, or by biochemical hyperandrogenism. Thus, for diagnosing of the syndrome, two of the following criteria would be necessary:
1) Oligo and/or anovulation and polycystic ovaries on ultrasound;
2) Clinical or laboratory evidence of androgen excess [4][6].
To get to these criteria, they considered the syndrome as an androgen excess disorder and its fundamental characteristics: menstrual or ovulatory dysfunction, hyperandrogenemia, clinical hyperandrogenism and polycystic ovarie. Further, the association pointed out that, the resulting phenotypes from the combination of such characteristics, as a group, but not necessarily individually, have insulin resistance and attendant risk of metabolic abnormalities [4][6].

**The Amsterdam ESHRE/ASRM—Sponsored 3rd PCOS Consensus, 2012**
most recently defined presence of 2 out of 3 criteria:
- Menstrual dysfunction and/or polycystic ovary;
• Hyperandrogenia and/or hyperandrogenism;
• The ultrasound showing a polycystic ovary [7].

Epidemiology
There are few epidemiological studies about the PCOS, mainly on population-based. The vast majority of published studies consist in data from clinical trials, many of them carried out in populations in endocrine care services or infertility clinics, with sample and classification problems, leading to difficulties in generalizability and comparability.

The United States and Europe are leading research into PCOS and more recently, some data were published by authors from outside this axis. The difficulties in classification PCOS and the diagnostic criteria to identify the main phenotypes have been discussed only in the last two decades, having difficulty finding a consensus [8]. It is estimated that worldwide, 105 million women between 15 and 49 years of age show PCOS, the same being responsible for 72% to 82% of causes of hyperandrogenism [9].

Symptoms
Symptoms include either excessive or absence of menstruation, Excessive hair growth or Hirsutism which occurs due to presence large no of male hormones, Acne, Drastic weight gain and one of the major symptom i.e. difficulties in conceiving [10-13]

Standard Diagnostic Assessment
A. History-taking
Specifically needed for menstrual pattern, obesity, hirsutism and the absence of breast development. If obese, the time of onset, progression and problems should be explored. Lifestyle parameters such as diet, exercise and smoking need evaluation, as do the age of onset and progression of hirsutism and/or acne. Any medications used and their effects on acne and hirsutism should also be considered. Family history should explore infertility, menstrual disorders, age of puberty and hirsutism in female relatives [14].

B. Physical examination
This includes general body habitus, obesity, body mass index, blood pressure, presence of acne, male pattern of baldness and evidence of acanthosis nigricans. The severity and distribution of hirsutism should be graded clinically. Girls with PCOS with marked hyperandrogenism such as clitoromegaly, deepening of the voice or a masculine body habitus should alert one to the possibility of virilizing adrenal/ovarian tumours or congenital adrenal hyperplasia [15].

C. Gynecologic ultrasonography
It looks for small ovarian follicles. According to the Rotterdam criteria, 12 or more small follicles should be seen in an ovary on ultrasound examination. The numerous follicles contribute to the increased size of the ovaries that is 1.5 to 3 times larger than normal [16].

**D. Laboratory tests**

Serum levels of androgens, including androstenedione and testosterone may be elevated. Dehydroepiandrosterone sulfate (DHEA-S) levels above 700-800 mcg/dL are highly suggestive of adrenal dysfunction. The free testosterone level is thought to be the best measure, with about 60% of PCOS patients demonstrating high levels [17].

2. The ratio of LH (Luteinizing hormone) to FSH (Follicle stimulating hormone) is greater than 1:1 (sometimes more than 3:1), as tested on day 3 of the menstrual cycle [18].

3. Fasting biochemical screen and lipid profile.

4. Two-hours oral glucose tolerance test (GTT) in patients with risk factors (Obesity, family history, history of gestational diabetes) may indicate impaired glucose tolerance (insulin resistance) in patients with PCOS [19].

5. Fasting insulin level or GTT with insulin levels (also called IGTT): Elevated insulin levels have been helpful to predict response to medication and may indicate patients who will need higher doses of metformin or the use of a second medication to lower insulin levels. A hypoglycemic response in which the two-hour insulin level is higher and the blood sugar lower than fasting is consistent with insulin resistance. A mathematical derivation known as the HOMAI, calculated from the fasting values in glucose and insulin concentrations, allows a direct and moderately accurate measure of insulin sensitivity (glucose-level x insulin-level/22.5) [20].

**E. Differential Diagnosis of PCOS**

Other causes of irregular or absent menstruation and hirsutism, such as hypothyroidism, congenital adrenal hyperplasia (21-hydroxylase deficiency), Cushing’s syndrome, hyperprolactinemia, androgen secreting neoplasms and other pituitary or adrenal disorders should be investigated. PCOS has been reported in other insulin-resistant situations such as acromegaly [19].

Management of PCOS Medical treatment of PCOS aims to lowering insulin levels, restore fertility, treat hirsutism or acne, restore regular menstruation and prevent endometrial hyperplasia and endometrial cancer. General interventions that help to reduce weight or insulin resistance can be beneficial for all these aims because they are believed to be the underlying causes [19].

**Diet regulation**
Where PCOS is associated with overweight or obesity, successful weight reduction is the most effective method of restoring normal ovulation and menstruation. Low-carbohydrate diet and sustained regular exercise may help. It has been recommended that a diet in which a significant part of total carbohydrates is obtained from fruit, vegetables and whole grain sources may be helpful. Vitamin D deficiency may play a role in the development of the metabolic syndrome because vitamin D is essential for formation of the hormones of the adrenal cortex. So, treatment of vitamin D deficiency is indicated in the management of PCOS [21].

**Medications**

Reducing insulin resistance by improving insulin sensitivity through medications such as metformin and thiazolidinedione have been an obvious approach and initial studies seemed to show effectiveness. The United Kingdom’s National Institute for Health and Clinical Excellence recommended in 2004 that women with PCOS and a body mass index above 25 be given metformin when other therapy has failed to produce results [22].

**Problems in Current Dietary Pattern**

If we take a look at the eating habits of the majority of the people, it can be clearly observed that there is a remarkably noticeable shift from eating fresh home cooked food to readymade, processed food on a daily basis. This diet lacks fiber, nutrients and minerals and so the amount of fiber intake has reduced drastically, especially in the developed countries. To add to the woes, there is an increased use of preservatives, chemicals, pesticides, chemical fertilizers from the initial stages of farming till the goods are packed and sold in the markets. Abundant use of plastics has also resulted in food and water contamination. In different ways, many chemicals, which are harmful and disrupt endocrine system, are getting into the human system. The general calorie intake has also shot up over the last couple of decades and this factor along with reduction in physical activities is causing the metabolic syndrome which in turn leads to PCOS. Exercise and diet can alter the metabolic syndrome associated with PCOS [23].

**Dietary management of polycystic ovary syndrome**

Research into the dietary management of PCOS is lacking, despite the fact that lifestyle modifications including diet, exercise and weight loss have been shown to be beneficial. A reduction in weight of as little as 5 % of total body weight has been shown to reduce insulin levels, improve menstrual function, reduce testosterone levels and improve symptoms of hirsutism and acne [24–40].

Approximately 50 % of women with PCOS are obese and this obesity is associated with a greater degree of insulin resistance, hyperinsulinaemia, lipid abnormalities, hyperandrogenism, hirsutism
and menstrual irregularities (41 - 46). Furthermore, there is a higher prevalence of abdominal body fat distribution in women with PCOS, even those of a normal body weight, and this increase in visceral fat has been shown to be associated with glucose intolerance and dyslipidaemia [47-48].

Most of the studies of dietary intervention in women with PCOS have focused on energy restriction rather than dietary composition per se, yet the weight loss seen in most of these studies has been small in comparison with the outcomes achieved. And while the incidence of insulin resistance is higher in women with PCOS who are obese, and weight loss clearly improves outcomes for these women, not all women with PCOS who have insulin resistance are overweight or obese. Studies have demonstrated a higher incidence of insulin resistance, IGT and type 2 diabetes in women with PCOS of normal weight [49-52], suggesting that dietary management of this condition must go beyond weight loss.

In most of the dietary studies in women with PCOS, improvements in metabolic and reproductive outcomes have been closely related to improvements in insulin sensitivity, suggesting that dietary modification designed to improve insulin resistance may produce benefits greater than those achieved by energy restriction alone.

With the high incidence of insulin resistance and IGT and the increased risk of type 2 diabetes in women with PCOS, research into the effects of diet and exercise on diabetes prevention is highly relevant to this group. The Diabetes Prevention Program achieved a 58 % reduction in risk of progression from IGT to type 2 diabetes with lifestyle modification, with the average weight loss a modest 5·6 kg [53]. These results were similar to the Finnish Diabetes Prevention Study, which also achieved a 58 % reduction in risk of diabetes with lifestyle changes including diet and exercise [54]. In this study average weight loss in the intervention group was 4·2 kg. While the Diabetes Prevention Program and Diabetes Prevention Study included only overweight and obese subjects, the Da Qing Study in China achieved a reduction in the incidence of diabetes with diet and exercise that was equally successful in normal-weight and obese subjects, suggesting that the benefits of diet and exercise were not related only to weight loss [55].

A recent study found that while the addition of metformin to a hypoenergetic diet improved menstrual function, there was no improvement in insulin sensitivity and hyperinsulinaemia [38]. Similarly, Hoeger et al. (2004) found no benefits on insulin sensitivity or glucose metabolism with the addition of metformin to lifestyle changes, although the combination did result in a greater weight loss and reduction in androgen levels compared with lifestyle changes or metformin alone.
Effects of dietary-induced weight loss:
Several studies have demonstrated a beneficial impact of weight loss on insulin resistance and hyperinsulinaemia in PCOS. In a first non-controlled study (24), 20 obese anovulatory women were evaluated, 14 with PCOS and 6 with the hyperandrogenism–insulin resistance–acanthosis Nigerians syndrome, before and after an average of 8 months on a hypocaloric dietary regimen. After a mean weight loss of 9.7 kg (from 85.9 ± 13.1 to 76.1 ± 14.1), glucose-stimulated insulin concentrations significantly decreased, consistent with an improvement in insulin sensitivity. The beneficial effect of diet-induced weight loss on fasting and glucose-stimulated insulin concentrations was subsequently confirmed by other controlled and non controlled studies [34]. Insulin sensitivity before and after weight loss has also been studied by the use of the euglycaemic hyperinsulinaemic clamp technique [26, 32, 46]. As reported in a recent review, weight reduction also has a potential benefit on lipid abnormalities, such as an increase in HDL-cholesterol and a decrease in triglyceride concentrations [34]. However, data are insufficient and long-term results are not available.

Which diet is best?
In search of the best diet to improve fertility and hormonal alterations in obese PCOS women, Moran et al. (2003) carried out a short-term study to investigate the effectiveness of a moderately energy restricted low protein–high carbohydrate (15 and 55% respectively) versus a high protein–low carbohydrate (25 and 40% respectively) diet. The authors found that both diets had a similar effect on body weight loss, glucose and insulin response to a standard meal test, with marginal differences in androgen concentrations in favour of the low protein–high carbohydrate diet. No other studies have investigated the efficacy of other different diets or of a selected manipulation of the macronutrient without energy restriction. Moreover, there are no studies on the potential benefit of short term versus long-term lifestyle manipulation, or on the effect of mild-to-moderate weight loss versus sustained weight loss. Issues for which more detailed data are needed also include the effect of lifestyle intervention in normal-weight PCOS women, whether some differences may exist according to ethnic variability, the effect of previous dietary habits, the effects of dietary manipulation on acne and hirsutism, pregnancy and neonatal outcomes, and, finally, long-term effects on diabetes and cardiovascular diseases.

Foods to AVOID:
A. High GI (Glycaemic Index) Foods:
Foods that have a high GI result in a quick rise in blood sugar levels. Insulin levels follow suit to deal with the glucose in the blood stream. Generally, high GI foods have been processed to
remove fibre and other nutrients so they may be tasty but they are high in calories while lacking in nutrients\[^{56}\]

Some examples of high GI foods to avoid: white rice, mashed potatoes, rice cakes, muffins and cakes.

**B. Dairy:**

We’ll get into more detail in a separate blog post, as it’s an important and often overlooked issue. Milk leads to a rise in testosterone levels. It contains a protein that limits normal testosterone processing in the body. With testosterone not being managed, testosterone levels just keep rising. As our testosterone levels are already prone to being high, dairy just makes the problem worse\[^{57}\]

**C. Soy Products:**

When I cut out dairy, I immediately turned to soy. Imagine my dismay when I found that soy has been implicated in delayed ovulation. Not enough studies have been done on the impact of soy on woman with PCOS and soy in small quantities may have little effect. However, I would not recommend soy products to women with PCOS, especially those that are trying to conceive\[^{58}\]

**D. Bad Fats:**

Saturated, hydrogenated and transfats are all fats that should be avoided. Saturated fats, found in red meat and dairy products, cause an increase in oestrogen production, hinder the absorption of some nutrients and can cause weight gain\[^{59}\]

The trans and hydrogenated fats, from cooked oil, margarine and processed foods, increase your risk of heart disease and diabetes, both of which we are already at risk of as a result of our PCOS.

So, cut down on red meat and get rid of the dairy, for all of the reasons also mentioned under the dairy section. Also, avoid those processed, fatty foods.

**Foods to INCLUDE:**

**A. Green Leafy Vegetables:**

Green, leafy vegetables have the most nutrients per calorie than any other food. They are rich in iron, calcium, potassium, and magnesium, as well as vitamins K, C, E, and many of the B vitamins.

Vitamin B in particular plays a vital role in managing PCOS symptoms. This is also worth a further discussion so I will write a separate post for it. Here are just some of the things that Vitamin B is responsible for: sugar and fat metabolism, thyroid function and hormone balance, amongst others. It plays a vital role in the management of PCOS\[^{60-72}\]

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B. Fruit:
Fruit is a rich source of fibre, vitamins, minerals and phytonutrients and should be enjoyed as part of a PCOS diet. Many women with PCOS are reluctant to eat fruit or avoid fruit as it can cause a spike in blood sugar levels and therefore insulin.

However, fruit still plays an important role in providing the nutrients we need to combat PCOS. So, try to eat fruit that has a lower GI and have a handful of seeds or nuts with your fruit as protein helps to regulate the sugar spike resulting from fruit.

Fruit with a low GI value include: cherries, plums, grapefruit, apples, pears, apples, dried apricots, grapes, coconut, coconut milk, kiwi fruit, orange juice, prunes.[73-77]

C. Coloured and White Vegetables
Brightly coloured vegetables are a rich source of anti-oxidants and should be included in a PCOS diet. Women with PCOS have been found to have a higher rate of oxidative stress. That is, physiological stress is placed on the body when dealing with high numbers of free-radicals. We need antioxidants to combat this oxidative stress.[78-83]

D. Organic, pasture-fed meat
This may be expensive but it is important that you eat good quality, lean meat if you do eat meat. Grass-fed meat tends to be leaner and contain less hormones than standard meat. Grass-fed is also important because livestock is often fed grain and feed that has been genetically modified or contains pesticides which are unhelpful for hormone balance and PCOS.[84-91]

E. Healthy Fats:
Not all fat is bad and healthy fats are essential for your PCOS diet.

Essential fatty acids are really important for maintaining the cell wall, which allows nutrients in, and toxins out. They are also vital for hormone balance, weight management and fertility.

These healthy fats are found in nuts and seeds, oily fish, avocado and olive oil so be sure to incorporate those into your diet.[92-96]

F. Supplements:
Following the diet described above will give you a good chance to get all of the vitamins and minerals you need but many women with PCOS are still lacking in some nutrients.

So, make sure that you take a good multivitamin and mineral supplement. It should contain the following Vitamins and minerals: Vitamin A, D, E, C, B1, B2, B3, B6, B12, folic acid, magnesium, iron, zinc, chromium, selenium and manganese.

This should provide you with a good supplemental basis. Many women with PCOS also take a Vitamin B complex, Vitamin D, chromium, Omega 3 and Ovasitol[97-103].
CONCLUSION:
PCOS is a complex condition, with diverse implications that include reproductive, metabolic, and psychological co-morbidities. Its clinical management should focus on lifestyle changes with medical therapy when required, as well as providing patients with support and nutritional education. Body weight loss is associated with beneficial effects on hormones, metabolism and clinical features. Diet modifications along with the treatment are necessary for greater improvement of metabolic and hormonal parameters in women with PCOS.

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