REVIEW ARTICLE

An evidence-based approach to nutrition and PCOS: The role of diet in polycystic ovary syndrome among women and adolescents

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Aim/Background: Polycystic Ovary Syndrome (PCOS) is a heterogeneous disorder characterized by hyper-androgenism and chronic anovulation. It is the most common endocrine disorder and metabolic heterogeneous disorder among reproductive-aged women, with likely genetic origin influenced by environmental factors including diet, lifestyle and social status. It aims to provide the clinical picture of the role of diet in polycystic ovary syndrome among women and adolescents in the world through documented cases.

Materials and methods: Using the databases of Science Directs, Research Gate, PubMed and Google Scholar, epidemiological studies focusing on the isolation and identification of cases linked to diet and polycystic ovary syndrome in women and adolescents between 2004 and 2022 were thoroughly evaluated.

Findings: A total of 512 articles regarding the prevalence of PCOS and nutrition in India and throughout the world can be discovered in the Google databases. The study took into consideration of 71 relevant articles for the purpose of the study.

Conclusion: Establishing the prevalence of relation between nutrition and PCOS is considered an important tool for developing evidence-based awareness among the public. Also, the existence of surveillance studies for these is an important step in assessing the health of the population as a whole.

Key Words: *PCOS; Women; Irregular menstrual cycles; Nutrition; Lifestyle changes*

INTRODUCTION

Among the reproductive-aged women, one of the leading hormonal problems is PCOS. Polycystic Ovary Syndrome (PCOS) is a hormonal disorder causing an enlarged small cyst on the outer edge. It is the most common endocrine disorder and metabolic heterogeneous disorder affecting 5%-10% of reproductive age, with environmental factors including diet, lifestyle and social status [1]. Polycystic Ovary Syndrome (PCOS) was indeed first described by Irving Stein and Michael Leventhal in 1935, hence sometimes referred to as "Stein-Leventhal syndrome." This condition is characterized by hormonal imbalances in women, leading to symptoms such as irregular menstrual periods, excess hair growth, acne and polycystic ovaries [2].

The prevalence of PCOS varies globally, with estimates ranging from 2.2% to 26%. According to the World Health Organization (WHO) report in 2012, approximately 116 million women worldwide are affected by PCOS.

PCOS occurs when an endocrine imbalance results in high levels of estrogen, testosterone and Luteinizing Hormone (LH) and decreases the secretion of Follicle-Stimulating Hormone (FSH). This syndrome is associated with a variety of problems in the hypothalamic-pituitary-ovarian axis and with androgen-producing tumours [3]. Menstrual irregularity is the most common manifestation of PCOS and is present in almost 80% of patients. The usual menstrual irregularities are oligomenorrhoea or secondary amenorrhea and sometimes primary amenorrhea or menorrhagia. However, 20% of women may have regular cycles despite ovulation [4].

LITERATURE REVIEW

Using the databases of Science Directs, Research Gate, PubMed and Google Scholar, epidemiological studies focusing on the isolation and identification of cases linked to diet and polycystic ovary syndrome in women and adolescents between 2004 and 2022 were thoroughly evaluated. The search term used to obtain the related literature were “nutrition and PCOS” “PCOS and obesity”, “women and nutrition”, “irregular menstrual cycles”, “nutrition and lifestyle changes”. The reference list of important related article was searched for further articles to be included.

DISCUSSION

A total of 512 articles were screened using the keywords related to the present study. After the exclusion of the non-qualified articles, 71 articles were found suitable for the study. Signs and symptoms of Polycystic Ovarian Syndrome (PCOS) include irregular or no menstrual periods, heavy periods, excessive hair on the body and face, acne pelvic pain, pregnancy difficulties and patches of thick darker, velvety skin. Associated conditions include type 2 diabetes, impaired glucose tolerance obesity, sleep apnea, heart disease, mood disorders, endometrial cancer, high blood pressure, dyslipidaemia, hyperinsulinemia and infertility [5]. It increases the risk of fatal deformities, miscarriages and complications during pregnancy including premature deliveries and neonatal complications [6]. Women with PCOS are more likely to suffer from depression, anxiety, poor self-esteem, altered coping abilities, strained relationships, decreased quality of life, disordered eating and psychosexual dysfunction [7]. Thus, PCOS is associated with short term and long-term presentations that may adversely affect women at varying stages of their life. Hence it is imperative to identify effective therapies for the prevention and treatment of the syndrome to reduce its health and economic burdens.

Prevalence of polycystic ovary syndrome among women and adolescents

Prevalence is the proportion of a population that has specific characteristics in a given time [8]. Polycystic ovarian syndrome is one of the most endocrine disorders of women in reproductive age affecting 5%-10% of all females and 4%-6% of adolescent girls and young women worldwide. Globally prevalence estimates of PCOS are highly variable ranging between 2.2% to 26%. World Health Organization (WHO) indicated that PCOS affected 116 million (3.4%) of women worldwide in 2012 [9]. In India, the prevalence of PCOS estimates is between 8.2% and 22.5% depending on the diagnostic criteria used. Boyle, et al., in their study stated that the global prevalence of

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PCOS varies from 4 to 21%, while the number of adolescents varies from 9.1 to 36% depending on the diagnostic criteria used [10]. According to Singh, et al., PCOS may initially enter adolescence, but the exact prevalence of PCOS in adolescence is unknown because of lack of data. The prevalence was determined to be 9.13 percent in a community-based study by Nidhi, et al. In their study, PCOS was found to be more prevalent in late adolescence (76.2%) than early adolescence. Kalavanthi, et al., confirmed the same in their research findings. Bharathi et al., identified in a survey on prevalence rate of polycystic ovary syndrome of 6% in South India, Chennai according to the Rotterdam criteria. Balaji, et al., in a pilots cross-sectional study in Tamil Nadu evaluated young adolescent females and found a prevalence of 18% for PCOS. They also concluded that urban women had a higher proportion of PCOS compared to rural women. Joshi et al., from Mumbai conducted an urban community based study, which showed that the prevalence of PCOS was 22.5% by the Rotterdam criteria and 10.7% according to androgen excess society criteria. A study carried out among medical students in private medical college in southern India using a modified Cronin questionnaire, which consisted of 10 elements, found PCOS to be a common disorder among participants. A Lucknow study was published in which women attending college with menstrual irregularity and hirsutism, in the age range of 18-25 years, were studied and it was reported that the NIH-based prevalence among participants was only 3.7% and a majority of them were lean [11].

According to international surveys, between 4 and 10 percent of women of reproductive age have PCOS. It is challenging to come to a firm conclusion since, depending on the criteria utilized in different research, PCOS prevalence was more or less high. In a study done in Korea among university students, 20% of PCOS cases were obese, compared to 38.5% of overweight or obese cases. However, the prevalence of PCOS among Korean university students was 49.9%. Nanjaiah, et al., conducted across-sectional study in Mysore to determine the prevalence of polycystic ovary syndrome among female students [12]. The study results concluded that girls with menorrhagia or oligo-menorrhoea had PCOS more frequently than girls with normal duration cycles and bleeding for 2-4 days which was statistically significant. The study also stated that prevalence of PCOS was more in the group of girls who did not have the habit of working out compared to often who had habit of doing walking or jogging for minimum 30 minutes a day. Ganie, et al., conducted a community-based study in various educational institutions across Kashmir valley in women aged 15-40 years were included using a multistage random selection process, women underwent a detailed clinical, biochemical, hormonal and sonographic evaluation to satisfy Rotterdam 2003 criteria [13]. The participants were also evaluated using NIH and AE-PCOS criteria. Out of 171 probable PCOS women who completed all biochemical, hormonal and sono-graphic assessments. Among these 171 women, 107 (64.8%) were diagnosed as PCOS by NIH criteria. Similarly, 131 (79.4%) women had PCOS by Rotterdam criteria and 127(76.9%) women had PCOS by AE-PCOS criteria. Based on extrapolation, the expected community prevalence of PCOS was calculated as 28.9% by NIH criteria, 35.3% by Rotterdam criteria and 34.3% by AE-PCOS criteria. The prevalence of PCOS is high among Kashmiri women and is probably the highest in a published series globally.

The above mentioned studies on Polycystic Ovary Syndrome (PCOS) have revealed several associations between PCOS and obesity, menstrual irregularities, geographic variation, physical activity, higher adolescence prevalence, also having an impact on quality of life [14]. These associations highlight the complex interplay of genetic, environmental and lifestyle factors in the development and manifestation of PCOS. Further research is needed to better understand these associations and their implications for prevention, diagnosis and management of PCOS [15].

Diagnosis of polycystic ovary syndrome

As a heterogeneous disorder, PCOS diagnosis is difficult and often retarded. As a diagnostic technique for patients exhibiting comparable symptoms, it is advised to use pneumoenographic imaging. When the size of the ovaries was 75% or more of the size of the uterine body or greater, the diagnosis was approved; when it was less than 25%, it was disapproved. The National Institutes of Health (NIH) criteria were devised in 1990 after a discussion among experts on the conditions necessary to define PCOS. According to them, two criteria must be met for a patient to be diagnosed with this syndrome: Oligo-anovulation and an excess of clinical or biochemical androgens. In 2003, the presence of polycystic ovary morphology on ultra-graphic imaging was added as a third condition defining the disorder [16]. Consequently, the diagnosis is considered valid if two of the three criteria are met, without other endocrinological conditions. The criteria known as "Rotterdam criteria" have been approved by the European society of human reproduction and radiological and the American society for reproduction medicine [17]. The prevalence of PCOS using Rotterdam criteria is as high as about 15% of women of reproductive age. In 2006 the Androgen Excess and the PCOS society (AE-PCOS) are mostly associated with androgen excess. Therefore, the diagnosis requires the presence of hyperandrogenism with signs of ovarian dysfunction, in the absence of other endocrinological etiology [18]. The Rotterdam diagnostic criteria were endorsed by international guidelines and consensus in by Teede, et al.

According to Alexiou, et al., there is a significant incidence of hyper androgenism among women with PCOS (78%) and an even higher prevalence among overweight women. Hirsutism, which is described as terminal hair proliferation emulating a male pattern, is a typical indicator of excess androgens in women with PCOS when examining hyperandrogenism symptoms. A diagnosis of hirsutism among women was often made using Ferriman-Galwey's modified system after obtaining a score of >8. Alopecia can be evaluated Ludwig's visual score. In the case of acne, no universally accepted visual evaluation is available. When clinical signs of hyper and rogenismare in accurate or missing, the calculated free testosterone, free androgenic index or bioavailable testosterone should be measured [19].

In case of irregular or missing menstrual cycles, a diagnosis of PCOS should be considered to be between 85% and 90% of women with oligomenorrhea and 30 to 40% with amenorrhea have PCOS [20]. Ovulatory dysfunctional is evaluated after 1year after the menarche and clinically results in irregular menstrual cycles, which are defined as shorten than 21 days or longer than 45 days for women aged 1 to 3 years after menarche and less than 25 to 35 days in women over 3 years of age after menopause. Ovarian ultrasound is an essential component of assisted human reproductive (ART), as assessing the number of anterior follicles predicts ovarian responses to medication along with the risk of ovarian hyperstimulation syndrome.

The NIH of HA (Hyperandrogenism)+OD (Ovulatory Dysfunction) are adequate for detecting women at high risk of insulin resistance and associated metabolic abnormalities. PCOM does not impact on the diagnosis or endocrine management of NIH PCOS. However ovularomen with HA have a low risk of insulin resistance and associated metabolic normalities, whether or not they have PCOM. As a result, medical endocrinologists should concentrate on determining the ovulation of an HA patient. Usually, OD is not a subtle discovery because it is accompanied by oligo menorrhoea (<6-8 rules per year). Since a significant minority of women reporting regular menstrual cycles can be ovulatory, however, it is prudent to confirm ovulation in this sub-group of HA patients. Glucose tolerance and lipids levels should be assessed in the NIH PCOS.

To establish diagnostic thresholds for PCO by FNPO, Jonard, et al., compared 214 well-characterized PCOS patients to 112 normal controls using transvaginal 2D ultrasonography (Follicle number per ovary). Patients with PCOS had a mean FNPO that was higher than controls when all 2-9 mm follicles were taken into account: 15.5 (range 10-27.5) versus 6.0 (range 4.5-10). They found that, with sensitivity up to 99% and specificity up to 75%, a mean threshold of 12 follicles between 2 and 9 mm afforded the best distinction between PCOS patients and healthy controls. The frequency of follicles between 2 and 5 mm in size increased in patients with PCOS, according to an examination of the subgroups, although clinical relevance.

Anti-Mullerian Hormone (AMH) is a part of the super family of transformative beta growth factor produced by ovarian granulosa cells. The major physiological roles of AMH in the ovary are prevention of recruitment of primordial follicles and modulation of the action of FSH in early follicular development. Since AMH concentrations are highly correlated to both biochemical HA and AFC (Antral Follicle Count),

studies have suggested that levels could be used as a tool to replace PCOM in the PCOS diagnosis. In a study, Eilertsen, et al., discovered that AMH may successfully replace PCOM for the diagnosis of PCOS and that using PCOM instead of AMH had the same diagnostic value as using AES and ROT criteria. These finding supports the replacement of AMH with PCOM, which demonstrated a comparable sensitivity to identify PCOS based on ROT and AES criteria. However, in comparison to the AES criteria, the specificity was not very high. AMH can thus successfully substitute PCOM in ROT and AES criteria and can even be used in NIH criteria to diagnose PCOS, as evidenced by the results of this study.

The role of diet in polycystic ovary syndrome

An unhealthy lifestyle, particularly a poor diet, leads to obesity and insulin resistance, dyslipidemia, glucose tolerance, type 2 diabetes, followed by the uncontrolled production of androgens (hyperandrogenism) which is the main characteristics of PCOS. As far as the association of obesity and insulin resistance with PCOS is concerned major dietary habits can play an important role in the prevalence and progression of PCOS.

Researchers have started to explore various dietary interventions to promote weight loss and simultaneously improve the eating behavior and quality of life of women with PCOS. Diet changes are considered the first line of therapy for those who have PCOS. A properly balanced reduction diet with low GI has proved to support the treatment of PCOS. Water soluble vitamins have antioxidant properties and contribute to metabolic transformation because regulators can be supplemented with a reduction diet, which is an advantage in treating of PCOS. Diets with low GI are becoming more and more acceptable for dietitians and patients in the management of PCOS. A short-term dietary alteration with low GI may slightly increase insulin sensitivity in women with PCOS. Moreover, in comparison to a normal GI diet, a low GI diet improves ovulation cycles in patients with PCOS and anovulation. A preliminary study has indicated that a low GI diet could reduce the risk of endometrial cancer by decreasing endometrial thickness and increasing the number of menstrual cycles in women with PCOS.

Moran, et al., evaluated the relationship between PCOS and specific nutrients, food categories or dietary patterns. In this regard, a thorough analysis of the majority of the included studies showed no discernible differences in menstrual, reproductive or metabolic traits with different food compositions. However, Lin and Lujan contend that a high-energy diet low in fibre, high in glycemic index foods and saturated fatty acids may affect the metabolic results in PCOS women. Stamets, et al., showed that adherence to two different low–energy diets (high in proteins and high in carbohydrates) improved reproductive function and that there were no differences between these two diets. Douglas, et al., examined the influence of a diet low in carbohydrates or high in mono-unsaturated fats compared to a standard diet. According to this study, a low-carb diet improved insulin sensitivity but had no impact on the levels of circulating reproductive hormones. Reduced glycemic load has been shown to help manage weight, improve glycemic control in diabetes, reduce dyslipidemia and increase HDL cholesterol levels. Dietary fibre can help regulate by showing its absorption into the circulation, which increase glucose tolerance. soluble fibre reduces the postprandial glucose response while insoluble fibre increases susceptibility. Fibre intake also been demonstrated to help manage weight potentially through increased post prandial satiety resulting in a reduction in overall calorie intake. Indeed it has been demonstrated that women who consume fewer dietary fibre gain more weight over time. Nadjarzadeh, et al., stated that dietary factors may have an impact on IR (Insulin Resistance), obesity and the expression of genes implicated in important metabolic pathways. According to Cunha, et al., study reports, Iranian women at higher risk for PCOS consumed more foods from western dietary patterns and consumed fewer foods from herbal diets. It was discovered that greater weights that can trigger the development or advancement of PCOS are connected to qualitative or quantitative nutritional deficits. Dietary Approaches to Stop Hypertension (DASH) as a type of diet that is rich in whole grains, vegetables, fruits and low-fat dairy products and low in carbohydrates, saturated fats and cholesterol, has beneficial effects on the BMI, antioxidant status, IR, annitricoxidein overweight or obese women.

A recent study showed the negative association between the severity of inflammatory profiles, IR and hyperandrogenemia with the Mediterranean diet in women with PCOS. Negative and positive associations have been reported between high glycemic index diet intakes and anti-inflammatory diets with a risk for PCOS, respectively. Furthermore, it has been reported that total protein dietary intake and energy intake from simple sugars are considerably lower in PCOS than in healthy women.

The Mediterranean Diet (Med Diet) is recognized as the healthiest dietary model. It has been included in international guidelines as a recommended healthy dietary pattern due to its unique characteristics, including regular consumption of unsaturated fats, fibre, low glycemic index carbohydrates, antioxidants and vitamins, as well as appropriate amounts of protein from animal sources. Many studies over several decades have shown that adopting the MedDiet pattern can protect against diseases such as obesity, cardiovascular disease, Type 2 Diabetes (T2D), Non-Alcoholic Fatty Liver Disease (NAFLD),cognitive interaction, breast cancer, chronic kidney disease MedDiet's beneficial mechanisms are to reduce inflammatory and oxidative stress markers and improve lipid profiles, insulin sensitivity and endothelial function, as well as anti-atherosclerotic and anti-thrombotic properties.

Pulses (e.g., lentils, chickpeas, split peas and dry beans) are rich in fibre and low in fat, contain high-quality protein and complex low GI carbohydrates and are important sources of vitamins and minerals like iron, zinc, folate, calcium, magnesium and potassium. Pulse consumption has been shown to improve cardiometabolic disease risk factors in women with PCOS. In a Kamran et al., study suggests that low calorie diet was a good option for weight loss in PCOS and reduced 7%-10% of weight in 6-12 months. Reduced calorie intake also helped other PCOS symptoms. A low-carb diet has resulted in a great improvement in weight and all the symptoms of PCOS.

Gopalan, et al., this study was a case-control study. The study population was women in the age group 15-45 years with complaints of PCOS and an age-matched control group. They were diagnosed PCOS cases using Rotterdam criteria and controls were age-matched women with PCOS. The average age of PCOS cases was 24.64 years. There was a statistically significant increase in the history of snacking with ingestion of high caloric and high fats food in PCOS cases compared to control women and this difference was also statistically significant. The results of this study suggest that PCOS is associated with the increased intake of food high in calories and saturated fat and those women who are obese or overweight are more likely to develop PCOS. Lifestyle modification like healthy diet and regular exercise should be the front-line therapy in PCOS women.

Lifestyle and management of PCOS

First-line therapy for PCOS includes lifestyle interventions, including nutrition education and physical training to prevent the risk of diabetes by supporting weight loss and improved glucose metabolism that helps to stabilize distressing disorders related to the condition of PCOS. Lifestyle treatment in overweight women with PCOS that leads to even small amounts of weight loss enhances reproductive biochemical results, surrogate markers of insulin resistance, adiposity and distribution of adiposity. There is not clear evidence based recommendations for the best food composition for PCOS. The significant benefits of exercise were described with improved anthropometric measures, insulin reactivity, lipid profile, cardiopulmonary function, inflammatory markers and the frequency of menstruation in women with PCOS after a structured workout. General recommendations on exercise include 150 minutes of exercise a week or 75 minutes of vigorous intensity a week. For moderate weight loss, preventing weight gain and greater health benefits, a minimum of 250 minutes per week of moderate and 150 minutes per week of vigorous activity is recommended. The effectiveness of lifestyle programs seems to be enhanced by incorporating behavioral strategies such as goal setting, self-monitoring, stimulus control, problem solving, assertiveness, slower eating, behavioral changes and relapse prevention to optimize weight management, healthy

lifestyles and emotional well–being. Nutritional therapies with an appropriate diet are effective in recovering metabolic disorders in obese women with PCOS. Intake of fiber and less trans fats are the primary predictors of metabolic improvement and weight management. Lifestyle intervention strategies are still considered a better alternative to pharmacotherapy for overweight women with ovulating infertility. A number of clinicians and plans consider lifestyle interventions to be the primary treatment for overweight and obese women with PCOS. Lifestyle alteration is considered to be an excellent rehabilitation for PCOS and metabolic disorders. Weight management in obese PCOS women is associated with reduced and Rogen hormone and normalization of menstrual cycles. Quality of life can be enhanced by lifestyle management and depression or anxiety in obese and overweight women who have PCOS.

PCOS is always linked to obesity. It can cause late pregnancy, miscarriages, pre-eclampsia and diabetes caused by pregnancy. Initial management of the PCOS consisted of adjusting diet and exercise to manage insulin resistance. 30 minutes of regular exercise for 3 days a week is said to be good for weight loss. Physical activity leads to improved symptoms of PCOS. In a Nybackaet, et al., study the effect of lifestyle change on PCOS was examined by reducing fat consumption with appropriate physical activity has led to improvements in metabolic disturbance. Compared with two groups one with diet and exercise did not succeed in their exercise habits because of their upper body strength. In the case of only the exercise group hsCPR (high sensitivity C–Reactive Protein) reduced the diet to more fibre and low fat, with exercise or without exercise always performed metabolic complications. Changing the diet in groups with more fibre and low fat was observed and all the fat storage and fat in the body began to use and decrease, BMI decreased and size also decreased as well as, except in the exercise group. In the exercise group, the upper body fat is reduced. Modifying the lifestyle of obese PCOS results in a reduction of fat and all other symptoms related to obesity and PCOS such as blood pressure, metabolic disturbances and insulin resistance. Still, the diet should contain more fibre, low fat and refined low-carbs. Mavropoulus, et al., investigated the effect of a 6-month lifestyle change to improve diet and increase exercise in obese infertile women, some of whom had PCOS and reported improved self–esteem and decreased depression and anxiety scores after 6-10 kg weight loss. It is also proven that independent exercise provides many psychological benefits, including improved mood, self-esteem, body satisfaction, overall quality of life and mental wellness and reduction of depression and anxiety symptoms. The role and effect of lifestyle alteration is well documented in the documentation. These non-pharmacological measures such as diet and exercise are recommended as primary treatment in oligo menorrhea, hirsutism, infertility and obesity in PCOS by the majority of endocrinologists and gynecologists. Physical activities have been widely known to induce oxidative metabolism in the tissue and the oxidative metabolism of the ovary is a stimulant for follicular development.

According to Maiya, et al., physical activity should be the primary course of treatment for weight loss because there are no known negative side effects. Gradual aerobic exercise is a particular technique for reducing body weight in PCOS-afflicted obese infertile women. Additionally, it promotes ovulation, increases pregnancy rates and reduces cyst size. Exercise is well recognized for enhancing a variety of health outcomes, such as protection against the onset of diabetes and cardiovascular disease, as well as morbidity and mortality reductions and an increase in psychological benefits. According to Wahrenberg, et al., improving the appearance of PCOS only requires a minimal weight loss (5-10 percent) over four weeks. Therefore, in overweight women with PCOS, weight loss is a desired result to treat both short-term metabolic healths. Decreases in testosterone levels, the free androgen index, belly fat, blood sugar, blood lipids and insulin resistance all support weight loss with calorie restriction. Additionally, it enhances fertility, ovulation and menstrual cycle regularity. Felver, et al., in their study demonstrated that exercise intervention (yoga) was linked to a significant improvement in the FG (Ferriman Gallwey) score and menstrual cycle irregularity, two clinical symptoms of PCOS. Exercise also markedly reduced the amounts of LH (Luteinizing Hormone), FAI (Free Androgen Index) and AMH (Anti-Mullerian Hormone) in the serum. Additional, this study demonstrated a considerable improvement in TG levels following exercise intervention, although there were no changes in the levels of other metabolic indicators. Yoga is an alternate kind of exercise that may help improve adolescent anxiety and mood as well as ovarian morphology in PCOS adult women.

CONCLUSION

It can be inferred from the review that there is no permanent cure for PCOS, but with a proper dietary management, lifestyle modification controlling it lowers risks of infertility, miscarriages, diabetes, heart disease and uterine cancer. Most endocrinologists and gynaecologists advise using non-pharmacological treatments including diet and exercise as first-line therapy for PCOS-related obesity, hirsutism, oligomenorrhea and infertility. A key component of PCOS management is changing one's lifestyle, with an emphasis on nutrition, increased physical activity and behavioural therapy. When combined with a balanced diet, antioxidants can help treat PCOS since they play a role in metabolic transition as regulators. Furthermore raising awareness among both women and adolescents remains crucial for early diagnosis, effective management and improved quality of life.

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