

Review Article

Effects of Lifestyle on Fertility in Women with Polycystic Ovarian Syndrome

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Abstract

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting reproductive age women worldwide. Women with PCOS experience absent or infrequent menses, infertility, acne, and excess hair growth, and ultrasound images show enlarged multicystic ovaries. Symptoms of PCOS include the endocrine system and reproductive signs which occur in the shape of amenorrhea or oligomenorrhea, hirsutism, obesity, acne, male pattern hair loss and reproductive disorders. IR is found in women with PCOS irrespective of their weight though it is more common with increasing weight and waist circumference (WC), which is especially significant as PCOS women are more likely to be overweight and have central obesity compared to the general population. Overweight and obesity affect reproductive capacity in the general population as well as in subfertile couples. Ovulatory subfertile women with a body mass index (BMI) of 29 kg/m² or higher than 29kg/m² have 4% lower pregnancy rate per kg/m² increase per year, compared to ovulatory subfertile women with a BMI below 29. Lifestyle modification is widely accepted as a first line of treatment for women with PCOS to optimize their health before and after with any fertility treatment. Weight loss and lifestyle management have been shown to improve mood states and reduce depressive symptoms in overweight and obese women without PCOS. This provided evidence that although weight loss is important, dietary composition may also be an influencing factor.

Keywords: Polycystic ovarian syndrome; Obesity; Fertility; Lifestyle.

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting reproductive age women worldwide [1]. Women with PCOS experience absent or infrequent menses, infertility, acne, and excess hair growth, and ultrasound images show enlarged multicystic ovaries [2]. Infertility is defined as inability to conceive after 12 or more months of unprotected intercourse; it commonly affects 13%–15% of couples worldwide [3,4]. PCOS accounts for 6% to 10% of infertility cases based on the USA National Institutes of Health criteria [5]. The therapeutic modalities of PCOS target the anovulatory infertility of PCOS. Anovulatory conditions are usually treated with lifestyle modifications [4].

This syndrome is characterized by irregular menstruation, polycystic ovaries and hyperandrogenism, insulin resistance, and obesity that is observed in 5 to 20 percent of women depending on the diagnostic criteria used

[6]. Symptoms of this syndrome include the endocrine system and reproductive signs which occur in the shape of amenorrhea or oligomenorrhea, hirsutism, obesity, acne, male pattern hair loss and reproductive disorders [7]. The actual cause of PCOS is unknown and probably stems from a combination of factors such as genetic factors, exposure to high levels of androgen prenatally, epigenetic factors and environmental factors. Various environmental factors play a fundamental role in the occurrence and treatment of this syndrome, among which dietary pattern, physical activity, smoking and stress could be pointed out [8, 9].

Though the aetiology of PCOS is yet to be fully elucidated, insulin resistance (IR) appears central to its pathogenesis, resulting in disordered folliculogenesis and increased metabolic risk most classically presenting as metabolic syndrome (MbS) [10]. IR is found in women with PCOS irrespective of their weight though it is more common with increasing weight and waist circumference (WC) [11],

which is especially significant as PCOS women are more likely to be overweight and have central obesity compared to the general population [12]. Despite the well-established benefits of regular physical activity, and its recommendation as a corner stone for PCOS management, many overweight women with PCOS do not engage in regular exercise [13]. Two important mediators of exercise behavior change are the perceived benefits and barriers of exercise, which can positively and negatively influence participation, respectively [14].

Obesity exacerbates the incidence, prevalence, and severity of PCOS, while weight loss has been shown to improve reproductive, metabolic, and psychological features in PCOS [15]. Obesity affects women across the continuum of their reproductive years, beginning in adolescence with earlier menarche in obese girls [16]. Obesity contributes to menstrual irregularities and oligo/anovulation, lower conception rates, reduced response to assisted reproductive technologies (ARTs), and higher rates of pregnancy complications [17,18]. Overweight and obesity affect reproductive capacity in the general population [19] as well as in subfertile couples [20]. When Ovulatory subfertile women with a body mass index (BMI) of 29 kg/m² or higher than 29kg/m² have 4% lower pregnancy rate per kg/m² increase per year, compared to ovulatory subfertile women with a BMI below 29. Since childhood obesity is increasing, most notably among girls, a significant increase in obesity related subfertility can be anticipated in the future [21].

Lifestyle management is considered as the first line therapy in PCOS women for prevention of weight gain and for weight loss [22]. As outlined in a 2013 ASRM committee opinion “Optimizing natural fertility,” states that “there is little evidence that dietary variations such as vegetarian diets, low-fat diets, vitamin-enriched diets, antioxidants, or herbal remedies improve fertility [23]. Previous studies have shown that dietary patterns rich in these B vitamins are associated with increased chances of pregnancy and decreased chances of adverse pregnancy outcome [24]. The present review focuses on the role that diet plays in mitigating chronic low-grade inflammation and the downstream effects on reproductive outcomes in women with polycystic ovary syndrome (PCOS) [25].

Weight loss and lifestyle management have been shown to improve mood states and reduce depressive symptoms in overweight and obese women without PCOS [26,27]. There were a large number of small (one or two-component) studies demonstrating that losing 5 to 10% of initial body weight improves reproductive, metabolic and psychological features in PCOS women [28]. Two studies investigated the effect of 6 month lifestyle modification aimed at improving diet and increasing exercise in obese infertile women, some of whom had PCOS, and reported improved self-esteem and reduced depression and anxiety scores after a 6–10 kg weight loss [29,30]. Two pilot studies have also investigated the effects of dietary restriction on psychological outcomes in obese women with PCOS [31, 32] and with one observing a trend for improvements in HRQOL after 24 weeks on a low-carbohydrate ketogenic diet [32]. Another study reported that a 16-week high-protein diet significantly improved depression and self-esteem, whereas despite similar weight loss (7–8 kg), the high-carbohydrate diet did not [31]. This provided evidence that although weight loss is important, dietary composition may also be an influencing factor.

Literature search strategy

Search strategy and data bases

We conducted a systematic literature review, with eligibility criteria and search strategy based on Cochrane library. The data bases searched are PubMed, BMC, Science direct and Sage Journal. A two- phased search strategy was performed with an initial search to establish primary search terms followed by a second systematic search in all relevant data bases using the search terms. Search included the following keywords: polycystic ovarian syndrome, obesity, infertility, lifestyle management. This search was conducted to identify relevant primary articles and studies on polycystic ovarian syndrome. Studies which were published from 1995 were searched and collected. A Systematic search of the literature was also conducted to identify relevant systematic reviews (only recent reviews of potential relevance were considered).

Selection criteria**Inclusion criteria**

Type of study: Randomized control trials, systematic reviews and cross over trails were considered.

Study population: All women with PCOS, obesity suffering with fertility problems are included.

Type of interventions: Interventions related to the diet and life style changes in PCOS and obese women were included.

Reports related to the effect of lifestyle on PCOS and obese women were also included.

Exclusion criteria

Exclusion criteria includes women with co-morbidities including hypertension, renal failure, placental hemorrhage and studies on surgical treatments, reviews like narrative reviews, opinions or editorials, reports published as meeting abstracts. We also excluded studies related to pharmacological treatment of PCOS, obese women, infertile women.

Data extraction

Data extraction included Information about 1) Study information (demographic details and year), 2) Type of study (Systematic review, RCTs and cohort studies), 3) Intervention (diet and life style changes), 4) Participants (PCOS and obese and infertile women), 5) Search strategy (search terms, inclusion and exclusion criteria)

PCOs and fertility

The prevalence of PCOS in the female population is 5% to 10% of premenopausal women, that prevalence rate increases to 50% in women who are considered to be subfertile. These women typically require assistance in achieving pregnancy, including lifestyle changes, laparoscopic ovarian drilling, or ovulation induction via medications. In some cases, more complex intervention is required, such as controlled ovarian hyper stimulation or in vitro fertilization (IVF) [33]. Most available data suggest that anovulation in PCOS is not the consequence of increased androgen ovarian secretion. Although patients with the classic National Institutes of Health anovulatory phenotype tend to have higher androgen levels than patients with the hyper androgenic ovulatory phenotype [34, 35]. High androgen

levels may be found in patients with no PCOS without determining anovulation [35, 36]. It has been suggested that the arrest of antral follicle growth and anovulation are the consequence of the derangement of early follicle development [37]. It has been shown that granulosa cells cultured from follicles derived from anovulatory women with PCOS are hyper responsive to follicle-stimulating hormone (FSH) in terms of estradiol production [38, 39]. When granulosa cells from ovulatory patients with PCOS were evaluated, these cells behaved normally in terms of estradiol response to FSH and responded to LH only when taken from a larger dominant follicle [40]. On the contrary, granulosa cells taken from anovulatory PCOS tended to be hyper responsive to FSH and in some instances responded to LH also when these cells were taken from small (3–4 mm) follicle. It is believed that oocyte developmental competence and the embryos resulting from fertilization are altered in women with PCOS, compared with women without PCOS [41]. There are multiple serum and follicular factors that are reportedly altered in women with PCOS that may be responsible for this poor embryonic development and reduced implantation.

Obesity and fertility

Obesity is associated with PCOS and adversely affects reproduction. Evidence of adverse effects includes increased rates of anovulation, fertility treatment failure, pregnancy loss, and late-pregnancy complications in overweight women [42]. Helping overweight women with PCOS achieve weight loss is essential to their long-term health, especially when they are experiencing infertility, because the loss of as little as 5% to 10% of total body weight has been demonstrated to restore ovulatory and menstrual function [43]. In working with patients, we discuss that in the case of PCOS there are good data that as little as a 5% loss of body weight is associated with improved ovulatory function, although at higher BMIs more weight loss may be required [44, 45]. In a study investigating serum PUF- As in women undergoing IVF, we found that women with an increased linoleic:a-linolenic ratio had a higher chance of pregnancy compared with women with a lower linoleic:a-linolenic ratio (relative risk [RR] 1.52, 95% confidence interval [CI] 1.09–2.13) [46].

Lifestyle and PCOs

Lifestyle management targeting weight loss (in women with a body mass index (BMI) ≥ 25 kg/m² (overweight/obese) and prevention of weight gain (in women with a BMI 18.5-24.9 kg/m² (lean) should include both reduced dietary energy(caloric) intake and exercise should be first line therapy for all women with PCOS [47]. Most anovulatory women with PCOS become ovulatory when they lose weight, and an increase of body weight may transform an ovulatory woman with PCOS into an anovulatory patient with PCOS [34, 48]. This present study takes a multi-disciplinary approach by incorporating measures from nutrition, physiology, kinesiology, psychology, and reproductive medicine. This approach is allowed for a comprehensive integration and association of the various components of PCOS which may lead to a better understanding of this multi-faceted syndrome. The inclusion of Kinesiology in this study produces unique data sets such as: the use of accelerometers to quantify levels of activity which have been determined via self-reported questionnaires in previous reports [49, 50] 7-day activity records [51] physical activity recall [52] interviews [53] and Pedometer [54]. There is a paucity of physical activity data using accurate and objective measures in women with PCOS [55] and the present study utilizes information obtained using both physical activity.

Preconception counseling

Women with PCOS should receive education and advice regarding:

- **Weight**
 - ❖ Encourage regular self-monitoring of weight
 - ❖ Routinely assess weight, BMI, and waist circumference in primary care
 - ❖ Focus on prevention of weight gain in young women and inform on reproductive features as well as metabolic complications
 - ❖ Recommend achievable goals
 - ❖ Encourage small incremental sustainable changes
 - ❖ Incorporate regular physical activity into daily routine
 - ❖ Provide management options for excess weight
 - ❖ Provide access to multidisciplinary treatment where needed

- ❖ Ensure ongoing support
- **Strategies to optimize fertility**
 - ❖ Lifestyle measures (healthy balanced diet, regular exercise, healthy weight)
 - ❖ Family planning (optimal age at family initiation)
- **Screening for metabolic complications**
 - ❖ 75 g oral glucose tolerance test for dysglycemia
 - ❖ Monitor blood pressure and treat if needed
- **Smoking cessation [56].**

Lifestyle and obesity

Daily physical activity and dietary changes together with weight loss can help restore ovulation and enhance fertility for overweight and lean women with PCOS by increasing insulin sensitivity and thus lowering androgens [57]. Polyunsaturated fatty acids (PUFAs) play an important role in reproductive processes, and cellular levels of these fatty acids are affected by diet [58]. Importantly, the effects of altered PUFA concentrations or omega-6:omega-3 PUFA ratios on normal reproductive processes must be more fully understood before recommending dietary interventions to patients [46]. Exercise participation of at least 150 minutes per week should be recommended to all women with PCOS, especially those with a BMI 25 kg/m². Of these 150 min, 90 min per week should comprise of aerobic activity at moderate to high intensity (60% - 90% of maximum heart rate) to optimize clinical outcomes [47].

The macronutrient composition of weight-loss diets

The two studies assessing the effect of low-carbohydrate diet (40% vs. 55%) in women with PCOS found no significant differences in weight loss, metabolic /endocrine profiles [59, 60]. In a short term study, the effects of a low carbohydrate diet (43% energy) and rich unsaturated fatty acids (17% energy) was compared to a standard diet (low-fat and high carbohydrate) and revealed a reduced insulin levels after a low carbohydrate diet; however, no significant changes in insulin sensitivity or sex hormones was reported [61]. Those diets rich in unsaturated fatty acids and polyunsaturated fatty acids (PUFA) resulted in a significant increase of Pregnanediol 3-glucuronide in women with PCOS, though only 2 out of 17 women showed signs of ovulation. Moreover, the levels of LH,

FSH, SHBG, DHEAS and testosterone did not change [62]. Limiting energy intake, independent of weight loss, led to improved reproductive parameters [60]. Recently, an interest has been observed regarding the use of high protein diets among the ones who wish to lose weights and control diabetes, as well as among women with PCOS. However, in some studies there is little evidence confirming the beneficial effects of such diets on insulin resistance and in some studies, it has also been reported that such foods will aggravate insulin resistance and impairment of glucose metabolism [63,64].

Lifestyle and fertility

Lifestyle modification is widely accepted as the first line of treatment for women with PCOS to optimize their health before and concurrent with any fertility treatment [22]. In fact, Mahoney et al (2014) [47] studied women diagnosed with PCOS and fertility challenges and concluded that individualized comprehensive treatment plans guided by motivational interview techniques that are integrated into primary care and reproductive medicine visits are cost-effective approaches with lifestyle modification. Lifestyle management, including diet and exercise programmes, should be used throughout the lifespan in women with PCOS to optimize health benefits generally and also to alleviate symptoms such as infertility [47].

Conclusions

PCOS, Polycystic ovary syndrome is common disease consisting of obesity, insulin resistance, infertility and polycystic ovaries. Ways to manage insulin resistance, obesity, infertility by lifestyle modifications and maintain stress management techniques, engaging in daily physical activity, adhering to medication and supplement recommendations, and following a healthy balanced meal plan. While lifestyle management is recommended as first line treatment of PCOS and maintain weight. Weight loss should be targeted in all obese and overweighted women with PCOS through reducing caloric intake by embellishing the adequate the adequate nutritional intake and healthy food choices irrespective of dietary resources. It has shown that the PCOS patients should reduce and control their weight and needs to be improved. Possible suggestion include:

Referral to dietician for all obese and overweighted patients; small group seminars in order to inform PCOS patients; Dietary and lifestyle modifications.

Conflicts of interest

The authors declare no conflict of interest.

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