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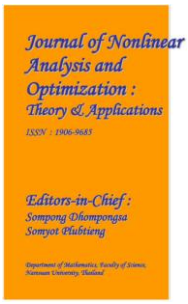

INSIGHTS AND PERSPECTIVES ON POLYCYSTIC OVARIAN SYNDROME: A NARRATIVE REVIEW

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ABSTRACT
Polycystic ovarian syndrome (PCOS) is a hormonal disorder recognized as a primary cause of female infertility worldwide. Women afflicted with PCOS exhibit elevated levels of male hormones, disrupting the delicate balance of female hormones crucial for ovulation. Characterized by enlarged ovaries containing multiple small cysts, PCOS manifests through various clinical presentations such as ovulatory dysfunction, polycystic ovaries, and hyperandrogenism. Conventional treatments often entail side effects, and a considerable portion of patients remain unresponsive to these measures. Consequently, there exists a demand for complementary therapies capable of mitigating PCOS symptoms without adverse effects. Homeopathy, a complementary medical system, has demonstrated effectiveness in addressing diverse ailments, including PCOS. This review aims to explore the positive outcomes associated with individualized homeopathic treatment in managing PCOS, underscoring its potential as a valuable therapeutic approach for this condition.

KEYWORDS:
Dysfunction, Homeopathy, Hyperandrogenism, Individualized, Infertility.

INTRODUCTION:
PCOS is the acronym for polycystic ovarian syndrome. It is the most common endocrine disorder of women in their reproductive period manifested by irregular menstrual cycles and polycystic ovaries, excess unwanted hair and baldness, although not all patients have all these features. The term ‘polycystic’ means ‘many cysts’, and PCOS gets its name because of the clusters of small, pearl-size cysts in ovaries. These cysts are fluid-filled bubbles (called follicles) that contain eggs that have not yet been released because of the hormonal imbalance. (1) Many women with PCOS demonstrate challenges to feminine identity and body image due to obesity, acne and excess of unwanted hair; also, infertility and long-term health-related concerns that compromise the quality of life and adversely affect mood and psychological well-being. Some authors have shown that women who have PCOS are more prone to depression, anxiety, low self-esteem, negative body image and psychosexual dysfunction. (2).
PCOS is also called as Stein Leventhal syndrome, after its description given by two doctors in 1935. They described it as a condition in which ovarian follicles does not develop properly because of hormonal imbalances (3). According to the National Institute of Health Office of Disease Prevention,

PCOS affects approximately 5 million women of child bearing age. Research suggests that 5-10% of females at 18 to 44 years of age are affected by PCOS making it the most common endocrine abnormality among women of reproductive age. Many studies conducted show that PCOS is hereditary; women with family history of PCOS are 30% more likely to develop PCOS (4). According to study, PCOS is affecting approximately 6-7 percent of the population around the world.

Prevalence: Prevalence of PCOS in India ranges from 3.7 to 22.5 per cent depending on the population studied and the criteria used for diagnosis. In India PCOD may affect 35% of women with symptoms like irregular period, heavy bleeding, dysmenorrhea, weight gain and unusual hair growth. The symptoms of PCOS are obesity, irregular menses, hirsutism, metabolic disorders and hormonal disorders. (5).

Historical perspective: The description of the clinical picture had been reported in the literature before the twentieth century, but it has been recognized since 1935 as PCOS by the work of two American surgeons, Stein and Leventhal (6). After that, several publications have been made seeking for a single pathophysiological mechanism to justify PCOS. The syndrome affects globally a large number of women, ranging from 5 to 15% of the women during their reproductive years (7-8). Thus, the diagnosis is based on criteria of expert consensus, including panels promoted by the US National Institute of Health (NIH) in 1990 (9) and the Rotterdam consensus, organized by the American Society for Reproductive Medicine (ASRM) and the European Society of Human Reproduction and Embryology (ESHRE), in 2003 (10-12). The latest consensus is the one issued by the Androgen Excess and Polycystic Ovary Syndrome Society (AE-PCOS), which recommends that women should have clinical or laboratory Hyperandrogenism associated with chronic anovulation and/or polycystic ovaries images (6,7).
In 2020, performed a retrospective study that analyzed clinical and laboratory data of 462 women with PCOS treated at an outpatient clinic in a tertiary hospital in southeastern Brazil (9). Women with PCOS had a median age of 25.0 years (range: 21.0–29.0) and a median body mass index of 28.7 kg/m2 (23.9–34.0). The prevalence of insulin resistance was 55.0%, glucose intolerance 28.1%, and type 2 diabetes 4.1%. Dyslipidemia due to low HDL-C levels occurred in 60.5%, hypertriglyceridemia in 25.9%, and central obesity in 61.3%. In our study, the metabolic syndrome was present in 27.4% of women, and hypertension in 10.9%. Interestingly, the prevalence of the metabolic syndrome in normal weight, overweight, and obese women with PCOS was 17.6%, 22.6%, and 33.9%, respectively (9). The therapy may focus on these metabolic disorders (1). (45-47)

Etiology: PCOS can be described as an oligogenic disorder in which the interaction of a number of genetic and environmental factors determines the heterogeneous, clinical, and biochemical phenotype. (13). Although the genetic etiology of PCOS remains unknown, a family history of PCOS is relatively common; however, familial links to PCOS are unclear. A lack of phenotypic information prevents a formal segregation analysis. Nonetheless, the current literature suggests that the clustering of PCOS in families resembles an autosomal dominant pattern. (14) Environmental factors implicated in PCOS (e.g., obesity) can be exacerbated by poor dietary choices and physical inactivity; infectious agents and toxins may also play a role. (14). The reproductive and metabolic features of PCOS are sometimes reversible with lifestyle modifications such as weight loss and exercise (15).

Development of PCOS: History of PCOS, with the term PCOS being applied to ovarian morphology. Disturbances in menstrual cycle, undesired male pattern hair growth, and enlarged ovaries with many tiny follicles are common traits shared by seven women (52). Lateral investigators confirmed that bilateral cystic ovaries formed as a result of inappropriate hormonal stimulation. Because of the availability of clomiphene and follicle-stimulating hormone (FSH), medicinal treatment has surpassed surgical ovary excision (53). When surgical treatment, such as laparoscopic surgery, became more common and preferred. PCOS diagnosis from gonads and allows the brain to connect with the ovaries via hormones, which are ultimately responsible for species survival and reproduction. The HPO axis is influenced by hormonal, neuronal (internal) and environmental variables (i.e. external factors).

Through epigenetic variables, these factors have an impact on the developing brain and germ cells in the following generation at the start of pregnancy(48).
An ovary image has gotten easier because to ultrasound technology (60). Many women with polycystic ovaries who had moderate or no other symptoms of PCOS experienced an unexpected outcome (58). This gave rise to the term polycystic ovarian morphology, whose importance is still up for discussion. The universal adoption of the Rotterdam criterion has been contested. which includes oligo an ovulatory woman with polycystic ovarian morphology but no clinical or biochemical indications of Hyperandrogenism, is premature and will result in unwarranted diagnosis, laboratory testing, and perhaps lifetime consequences for these women (61). Even after so many years, the actual etiology of this condition is still unknown, and it is currently thought to be multifactorial, with a strong genetic component. Despite the fact that it is routinely detected in patients, insulin resistance (IR) is not included in any diagnostic criteria. (62).

Pathophysiology: Due to insulin resistance and its elevated level, the ovaries function disturbs that rises androgen level which leads to anovulation (16). The level of gonadotrophin-releasing hormone, follicular stimulating hormone (FSH), luteinizing-hormone (LH) and prolactin is also disturbed in case of PCOS (17). Apart from the environmental factors, there are genetic factors that are responsible for the etiology of PCOS. Its cause involves candidate genes, SNP's. According to databases PCOS etiology involves 241 gene variations (18). Polymorphism or any nucleotide change cause a defect in the transcriptional activity of a gene that leads to PCOS (19). Mostly genes that encode for the androgen receptor, Luteinizing Hormone receptors, Follicular Stimulating Hormone receptors, Leptin receptors are responsible (20). Gene defect perturbs the biochemical pathway and leads to dysfunction of an ovary. Polymorphism such as polymorphs, FSHR polymorphism, FTO polymorphism, VDR polymorphism, IR and IRS polymorphism, GnRHR polymorphism are found to be involved in PCOS cause (13). PCOS progression and severity increases with the increase in insulin level as well as an androgen. Hyperinsulinemia affects ovarian theca cells and raise androgen level. This condition reduces the hepatic biosynthesis of SHBG and IGFBP-1. Elevated androgen level, on the other hand, stimulates visceral adipose tissue (VAT) that generates free fatty acids (FFA's) which contributes in insulin resistance (21).

Clinical Features / Sign and Symptoms: PCOS patients have numerous cyst 8 mm in size in the sac of their ovary. More than 12 cysts are present in the ovary. About 70% of females are infertile because of this condition (22.23). As discussed above in PCOS condition, the level of male hormones i.e. androgen elevated that causes hirsutism and acne. There is an insulin resistance which leads to obesity and Type 2 Diabetes. This problem leads to an irregularity in the menstrual cycle that results in infertility. 20% of females often experienced sleep apnea. Depression and anxiety are common (24).

Table 1: Signs and Symptoms:

Symptoms (62)	**Associated With (62)**
Acne, Hirsutism, LH secretion(62)	Hyperandrogenism(62)
Infertility, Miscarriage rates are high. There are no periods. Bleeding excessively during periods, Ovulation does not occur in eggs. Periods of inconstancy(62)	Disrupted menstrual cycle(62)
Insulin sensitivity Intolerance to glucose Obesity Hyperlipidemia, Diabetes, Cardiovascular problems(62)	Metabolic disturbances(62)
Enlarged ovary with cyst(62)	Ovaries(62)

Anxiety, depression, irritation, mood swings(62)	Mental health(62)

Diagnosis:

This condition can be diagnosed on the basis of Rotterdam criteria i.e. irregular menstrual cycle, elevated androgen level, the presence of cysts (25). Diagnostic criteria of PCOS are portrayed in Table 2. (25)

Table 2: Diagnostic criteria of PCOS

NIH 1990(25)	Rotterdom2003(25)	AE- PCOS 2006(25)
Long lasting anovulation(25)	Oligo/ anovulation(25)	Biochemics clinical evidence of Hyperandrogenism.(25)
Hyperandrogenism(25)	Hyperandrogenism PCOS (25)	Dysfunction of ovulation Polycystic ovarian morphology(25)

Management: The medical management of PCOS can be broken down into four components, three of which are "acute" issues (control of irregular menses, treatment of hirsutism and management of infertility) and one that is more "chronic." This latter issue may be the most important but least remembered by patients and providers alike–management of the IR syndrome. "Acute" issues that need management may change, however, a continuous life-long management approach is important for the IR of PCOS. (32,33)

Control of Irregular Menses This cardinal feature of PCOS can be both a nuisance and a significant health risk to patients. Irregular menses can be embarrassing because of unpredictability and painful because the infrequent occurrence often leads to increased cramping with the heavier flow (26,27). Infrequent menstrual cycles also carry a 3-fold increased risk of endometrial carcinoma. (28) In general, four menses per year are required to control this increased risk. (29).

Weight loss itself can result in improvement in menses (34). Kiddy *et al.*, showed improvement in menstrual function in 9 of 11 patients (82%) with oligo menorrhea who lost >5% initial body weight (range 5.9 to 22%) on a 1000 kcal/day, low-fat diet over 6 to 7 months, whereas only 1 of 11 patients (9%) losing <5% body weight demonstrated such improvement. (30,49).

Treatment of Hirsutism Hirsutism can be measured and quantified by a variety of methods. However, the decision of if and when to treat should be based on the patient's perception of the excess terminal hair growth. A similar degree of hirsutism in two different patients may result in vastly different degrees of distress. When thought of simply, hirsutism can be managed in two ways: through medical means by decreasing the amount or blocking the action of androgens or by mechanical means (i.e., shaving, etc.). (30,32)

Medical Decreasing testosterone production Excess testosterone production is predominantly ovarian in nature and is caused by both increased luteinizing hormone stimulations from the pituitary and the effect of hyperinsulinemia at the ovary. By decreasing gonadotropin production and increasing sex hormone binding globulin (SHBG), oral contraceptives generally decrease bioavailable testosterone levels by 40% to 60%. (43) By improving insulin sensitivity (and thus lowering insulin. (56,57) Decreasing testosterone action as none of the above therapies will fully suppress testosterone levels, the additional method of blocking testosterone action is useful. (59)

Management of Infertility PCOS accounts for 75% of an ovulatory infertility. Additionally, if/when pregnancies do occur, the first trimester miscarriage rate is as high as 30% to 50%. (30) Successful medical management of infertility in these patients can be extremely rewarding to patients and physicians alike. Management of infertility can be difficult, however, and a team approach between the endocrinologist, gynecologist and, perhaps, reproductive endocrinologist should be stressed. An extensive review of the intricacies of infertility management of the patient with PCOS is beyond the scope of this review. (35,50)

Dietary management:

Advised to intake: Increase the diet of high-fiber carbohydrates gradually, food high in lean protein should be prioritized including foods high in monounsaturated and omega-3 fatty acid as well as lots of low glycemic index fruits and vegetables in the diet. Drink at least 2 liters of water, exercise regularly. Meals should not be skipped, (31,37,42) instead consume less amount of food in each meal.

Avoid: Patients with PCOD should avoid items that are already regarded as unhealthy in general. Here are a few examples such as refined carbohydrate sources include cakes, pastries and white bread. Fried food and fast food such as pizza and burgers, carbonated beverages, such as sodas and energy drinks. They are high in sugar, processed meats, such as salami, sausages, and hot dogs, cured ham and bacon, along with luncheon meat, margarine, shortening, and lard red meat like steaks, pork and hamburgers (42).

Exercise: Regular aerobic exercise helps to control PCOS. Without losing weight, aerobic exercise reduces insulin resistance and ovarian morphology in women with PCOS. Exercise causes changes in visceral fat and ectopic lipid in non-fatty tissues. Aerobic exercise performed for a short period of time at a moderate intensity improves ovulation and menstrual cycle management while also lowering weight and IR in young women with PCOS. (37,41,51).

Lifestyle Modification/Weight Loss weight loss reduces hyperinsulinemia and subsequently Hyperandrogenism (39,40,44).In the study by Kiddy et al. discussed earlier, about 40% of obese women with PCOS (mean body mass index (BMI) ~34 kg/m2) who lost >5% of initial body weight with caloric restriction achieved spontaneous pregnancy.(31) A more recent trial compared the effects of an energy-restricted diet (~1400 kcal/day) through either a low or high protein diet in 28 obese (mean BMI ~ 37 kg/m2) PCOS subjects over 12 weeks.(42) Subjects were also advised to increase exercise to a minimum of 3 times weekly though no information was reported as to the actual duration and/or intensity achieved. Average weight loss was 7.5% (with abdominal fat decreasing 12.5%), and 3 of the 20 subjects actively trying to conceive did so (two in the high and one in the low-protein group) for a rate of 15%. Thus, lifestyle modification needs to be stressed in the treatment of infertility. A 3 to 6-month trial of aggressive lifestyle modification may be a prudent first step before considering an insulin sensitizer. However, many patients will have difficulty in achieving weight loss. (36,38).

Homeopathic Therapeutics:(65) The common drugs coming up for PCOS according to its clinical presentation are, Thuja, Bryonia, Pulsatilla, Lycopodium and Apis Mellifica, Natrum Muriaticum, Kali Bichromicum Calcarea Carbonica, Sepia Officinalis, Lachesis Mutus, Radium, Bromium, Calcarea Fluoric, Calcarea phosoricum, Belladonna Colocynthis, Magnesium Phosphorica, Cimicifuga, Senecio, Thalaspium Bursa, Kreosotum, Sabina.

CONCLUSION:

As time has advanced, we have seen a lot of change in healthcare, particularly the shift from infectious to non-communicable diseases in India and the increase of maintaining causes. Thus it is imperative to explore treatment modalities to combat these obstacles to cure. In that endeavor, we present a varied approach to cases of Infertility due to PCOS, remembering Dr. Hahnemann's warning against making 'favourite remedies' as that puts the smaller and less proved remedies at a disadvantage.

"The true physician will be careful to avoid making favorites of certain remedies that he has happened to have found indicated rather often and has had the opportunity of employment with good results. Otherwise, less frequently used remedies that might be more homeopathically suitable, consequently more serviceable will often be neglected." Aphorism no.257, 6th edition of Organon of Medicine (68) This is apt for some of the smaller and lesser-known remedies. The characterizing value of locality is often underrated but the concept is age old from the time of Rademacher & Paracelsus. Boenninghausen in his grand essay, Dr. Drysdale & Dr. Burnett have elaborated the concept thus- "That the organ does indeed possess not only autonomy but hegemony, i.e. the organ is an independent state in itself & on the organism exercises an important influence." Dr. Burnett, in his book BEST OF BURNETT has stated: "where the organ ailing is primary to the organ use organ remedies in little material doses frequently repeated; where the organ ailing is of piece pathologically with that of the organism, use the homoeopathic similimum in high potency infrequently repeated. (69,70) The reason for selecting homeopathic medicine act on particular organ also.

To effect cure in pathological cases, and do so repeatedly, it is imperative to adhere to the cardinal principles of Homeopathy of individualization, single remedy at a time and minimum dosage but with evolution in disease patterns such as cases of resistant PCOS, a modern approach has been suggested that has been used successfully in treating multiple cases of Infertility due to PCOS. This enables faster results with ovulatory cycles and can be used to hopefully reduce the number of patients needing Assisted Reproductive Technology.

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