



RESEARCH ARTICLE

PCOS, THE MULTIFACETED DISORDER – AN EXPOSITION

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ABSTRACT

Polycystic ovary syndrome, or PCOS, is one of the most common endocrine disorder in women. It is a heterogeneous complex genetic trait of unclear aetiology. The prevalence of PCOS varies depending on the criteria used to make the diagnosis. Clinical manifestations of PCOS include oligomenorrhea or amenorrhea, hirsutism, and frequently infertility. Earlier it was thought of as a fertility problem, but it is now known that PCOS is a metabolic disorder like diabetes that can have serious health consequences, if not diagnosed and controlled. Risk factors for PCOS in adults include hereditary factors and environmental factors like physical inactivity, greater intake of junk food, obesity and its associated insulin resistance. Insulin resistance affects 50%–70% of women with PCOS leading to many comorbidities including metabolic syndrome, hypertension, dyslipidemia, glucose intolerance, diabetes and cardiovascular disease. Studies show that mental health disorders including depression, anxiety, bipolar disorder and binge eating disorder also occur more frequently in women with PCOS. Weight loss improves menstrual irregularities, symptoms of androgen excess, and infertility in patients with PCOS. Management of clinical manifestations of PCOS needs to be individualised and includes medication for menstrual irregularities and hirsutism along with effective approaches to nutrition and exercise to improve body composition, endocrine features, reproductive function and cardiometabolic risk profile. Proper diagnosis and efficient management is essential to prevent future metabolic, endocrine, psychiatric, and cardiovascular complications. This review article focuses on the various dimensions of PCOS.

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INTRODUCTION

'Polycystic Ovary Syndrome' (PCOS) also known as Stein Leventhal syndrome was first reported by Stein and Leventhal who, in 1935, described seven women suffering from amenorrhea, hirsutism, and enlarged ovaries with multiple cysts. It is now identified as a common, heterogeneous, heritable endocrine disorder affecting women of the reproductive age group. PCOS is presumed to be a common yet silent disease affecting thousands of women worldwide. The PCOS Awareness Association (PCOSAA) states that one out of every 10 women has the endocrine disorder. It is believed that over 10 million women worldwide are affected by this condition but unfortunately, about half of them aren't aware that they are affected. It is also becoming a serious health concern among Indian adolescent girls and young women. The incidence of PCOS appears to be rising or perhaps it is now being diagnosed more often. The aim of this review is to provide an overview of the current knowledge concerning PCOS as well as to shed light on the associated co-

morbidities and to emphasise the need for proper diagnosis and a holistic approach towards the care and management of PCOS.

Prevalence

The available data on the prevalence of PCOS among different populations is limited and varied. The worldwide prevalence of polycystic ovarian syndrome ranges from 2.2 to 26% (Nidhi *et al.*, 2011). In the US, PCOS affects about 6-8% of women of reproductive years; similar estimates prevail in Greece, Spain and the UK. The prevalence reported in some other countries are as follows: China: 6.3%; Sri Lanka: 6.1% Australia: 11.9 ± 2.4% (Knochenhauer *et al.*, 1998; Diamanti-Kandarakis *et al.*, 1999; Michelmores *et al.*, 1999; Azziz *et al.*, 2004; Kumarapeli *et al.*, 2008). The prevalence rate in India based on few studies seem to vary between 3.7% to 22.5% (Gill *et al.*, 2012) and 9.13% to 36% in adolescents only (Nidhi *et al.*, 2011). The rates of polycystic ovarian syndrome are reportedly high among Indian women compared to their Caucasian counterparts (Wijeyaratne *et al.*, 2002). According to Dr. Hrishikesh Pai (TOI, 2013), PCOS is seen in as many as 25 to 30% of young women and is a metabolic disorder that is estimated to affect approximately 10 percent of reproductive

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aged women. A study by Metropolis estimated the following region wise prevalence of PCOS: North India-18.62%; East India- 25.88%; West India-19.88% and South India-18%. It also reported an increasing trend of PCOS predominantly in the age group of 15 to 30 years (Indiatimes.com, Sept 7, 2015).

Definition

PCOS is a condition in which there is an imbalance of the female sex hormones in a woman, leading to changes in menstrual cycle, cysts in the ovary, infertility and other health problems. PCOS has been defined by the National Institute of Health and Rotterdam criteria as a hormonal disorder characterized by the presence of at least one polycystic ovary (presence of multiple cysts) accompanied by ovulatory dysfunction and excessive secretion of androgens (Yii *et al.*, 2009).

Diagnosis

Not everyone with ovarian cysts have PCOS, nor does everyone with PCOS have polycystic ovaries (PCO). A pelvic ultrasound is a major diagnostic tool but it is not the only one. The below Table 1 summarises the different diagnostic criteria of PCOS.

Table 1. Diagnostic Criteria of PCOS

NIH 1990	Rotterdam 2003	Androgen Excess Society 2006
Must Include	Two of the following 3	Must Include
Chronic anovulation	1. Oligo/anovulation	Ovarian dysfunction
Clinical and/ or	2. Clinical and/ or	Oligo/anovulation
Biochemical signs	Biochemical signs	Polycytic ovaries on USG
of hyperandrogenism	of hyperandrogenism	Androgen Excess
	3. Polycytic ovaries on USG	Hirsutism
		Hyperandrogenemia

The most commonly practiced diagnostic criteria among the Indian medical fraternity is the Rotterdam criteria. Based on the possible combinations of these criteria, four different phenotypes of PCOS have been identified (shown in Fig-1):

- **Type A:** hyperandrogenism (HA), chronic anovulation (CA) and polycystic ovaries (PCO).
- **Type B:** HA and CA
- **Type C:** HA and PCO
- **Type D:** CA and PCO.

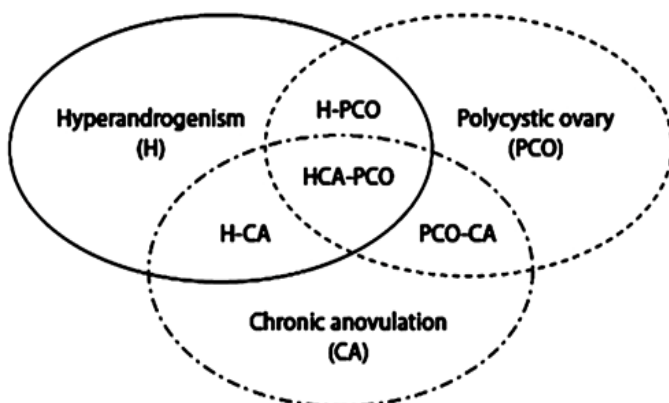


Fig.1. Phenotypes of PCOS

As per the suggestions of Consensus on women health aspect of PCOS, 2012, the diagnostic criteria of PCOS in adolescents should include all the three elements of Rotterdam criteria in which

- 1) oligomenorrhea should be present after two years of menarche or primary amenorrhea at the age 16 years;
- 2) polycystic ovaries on ultrasound along with ovarian size of more than 10 cm and
- 3) hyperandrogenemia should be present.

During the diagnosis of PCOS, it is important to screen all women to exclude other disorders like thyroid disease, prolactin excess and non-classical congenital adrenal hyperplasia, which mimic the symptoms of PCOS (Malik *et al.*, 2014).

Aetiology

PCOS seems to be a complex condition with an ambiguous aetiology. Factors such as heredity, greater intake of junk food, insulin resistance, low-grade inflammation are believed to play a role (Indiatimes.com, Sept 7, 2015). Though the direct cause of PCOS remains unknown; both environmental and genetic factors are implicated.

- Hereditary factors may include early age of sexual maturation, premature foetal development, and family history of PCOS among first-degree relatives.
- The environmental factors attributed include physical inactivity, obesity, and its associated insulin resistance. Insulin resistance which is of high prevalence in the Indian population has been consistently reported as a strong determining factor for the occurrence of PCOS in Indian adults and adolescents (Wijeyaratne *et al.*, 2011; Yii *et al.*, 2009; Diamanti-Kandarakis, 2006).

The fact that its clinical presentation varies so much among individuals is likely due to interactions of genetic and environmental factors.

Symptoms

Symptoms related to PCOS can begin at any age and may be widely varying, but more often, will include some or all the following:

- Irregular periods
- Hirsutism (increased hair growth) on the face, chest, stomach, back, thumbs or toes
- Ovarian cysts
- Acne, oily skin, or dandruff
- Weight gain or Obesity, particularly centred around the middle
- Thinning hair or hair loss in a classic male baldness patter (Alopecia)
- Infertility
- Abnormal bleeding from the uterus
- High blood pressure
- Patches of skin that are thick or dark, particularly in neck folds, armpits, folds in waistline, or groin (Acanthosis nigricans)
- Skin tags
- Pelvic pain
- Sleep apnea

However, there are women who will have few if any of these symptoms. The clinical presentation of PCOS varies widely. But when fully expressed, the commonly observed manifestations include irregular menstrual cycles, hirsutism (abnormal facial and skin hair growth), acne, infertility and frequently, obesity. The commonly observed menstrual disturbances in PCOS include oligomenorrhea, amenorrhea, and prolonged erratic menstrual bleeding. However, 30% of women with PCOS will have normal menses (Balen, 1995). Approximately 85%–90% of women with oligomenorrhea have PCOS while 30%–40% of women with amenorrhea will have PCOS. More than 80% of women presenting with symptoms of androgen excess have PCOS (Azziz *et al.*, 2004). Hirsutism is a common clinical presentation of hyperandrogenism occurring in upto 70% of women with PCOS (Fausser *et al.*, 2012). Hirsutism is evaluated using a modified Ferriman–Gallwey (1961) scoring system. Though acne is most common during adolescent phase of life, there is limited literature on adolescent androgenic alopecia.

Prognosis / Co-morbidities

PCOS can lead to an array of physiological and psychological morbidities if not properly managed. A common correlate of insulin resistance (IR) and obesity is prevalent in women with PCOS. Visceral rather than subcutaneous fat is a defining characteristic of PCOS. Numerous studies have documented that insulin resistance and hyperinsulinemia is common in both obese and lean women with PCOS, which increases the chance of the metabolic syndrome. This in turn places those affected at increased risk of diabetes, hypertension, dyslipidemia, endothelial dysfunction, reduced vascular compliance, sleep apnea, atherosclerosis, other cardiovascular diseases (CVD) and stroke and even gynaecological cancers, compared with age-matched controls (Sharma and Nestler, 2006). Studies have reported 10 times greater risk of developing Type 2 diabetes in women affected by PCOS (Nidhi *et al.*, 2011). Thus, PCOS adversely affects endocrine, metabolic, and cardiovascular health. Moreover, certain aspects of PCOS such as infertility, hirsutism, acne, and body dissatisfaction can also account for emotional disturbances in women with PCOS. Several studies have shown that emotional disturbances such as depression, mood swings, are more common in women with PCOS than among women without PCOS. Further, PCOS women are also more likely than non-PCOS women to suffer from social withdrawal, eating disorders, and anxiety disorders, with one study reporting that 34% of women with PCOS have clinically significant anxiety (Mansson *et al.*, 2008). Thus, several short and long-term psychosocial and physiological health problems are associated with PCOS.

Care and Management

Management of PCOS should encompass management of long-term consequences that have clinical and psychological effects on women with PCOS. Since the three main characteristics of PCOS (HA, oligo-ovulation and IR) become the precursors for its long-term consequences, management approaches targeted at them may potentially provide improvement in all aspects of the syndrome. Therefore, the primary treatments for PCOS include: lifestyle changes, medications and surgery, if needed (Lim *et al.*, 2011). Both non-pharmacological and pharmacological management strategies are crucial in overall management of PCOS. Non-pharmacological intervention in the form of lifestyle changes –

diet and exercise - that aim to reduce weight or insulin resistance can be beneficial as first-line treatment and as they address to what is believed to be the underlying cause. As PCOS appears to cause significant emotional distress also, appropriate psychological support may also be useful (Veltman-Verhulst, 2012). Pharmacological therapy (like oral contraceptives, metformin, prednisone, leuprolide, clomiphene, spironolactone, progestins, anti-androgens and insulin-sensitizing medications) reserved for androgenic suppression and regular menstruation, to improve insulin sensitivity or to promote weight loss are most likely to be beneficial when used early in combination with diet and exercise (Farshchi *et al.*, 2007; Malik *et al.*, 2014).

Diet and Exercise

Research has shown changing eating habits and getting more exercise helps to manage PCOS. Diet and exercise need to be tailored to the individual's needs and preferences. A low GI diet, in which a significant part of total carbohydrates is obtained from fruit, vegetables, and whole-grain sources, resulted in greater menstrual regularity than a macronutrient-matched healthy diet (Moron *et al.*, 2013). Interventions using dietary supplements like antioxidants to correct metabolic deficiencies in people with PCOS had been tested in small, uncontrolled and non-randomized clinical trials but the resulting data is insufficient to recommend their use (Huang and Coviello, 2012; Amini *et al.*, 2015). Weight loss is a crucial aspect of treating PCOS, as it not only helps to induce ovulation and eventual pregnancy but also reduces the possibility of developing chronic diseases associated with obesity that are prevalent in PCOS (i.e., diabetes, CVD). It also reduces bioavailable testosterone levels and thereby some PCOS symptoms (Moran *et al.*, 2003; Norman *et al.*, 2002). Regular exercise appears to engender improvements in ovulation rate and likelihood of pregnancy; the primary goals of PCOS management. In one study, a 6-month lifestyle program intervention including both diet and exercise counseling restored normal menstrual cycles in 60% of anovulatory and women with PCOS (Huber-Buchholz, 1999). A review comparing minimal or no treatment with lifestyle modifications (diet, exercise, behavioural or combined treatments) in patients with PCOS, reported improved body composition, HA and IR in women with PCOS (Moron *et al.*, 2013). Thus, effective approaches to nutrition and exercise improve endocrine features, reproductive function and cardiometabolic risk profile.

Conclusion

Findings make it more than evident that PCOS is a highly multifaceted syndrome. Proper diagnosis and management of PCOS is essential as PCOS has many potential metabolic risks if not managed appropriately (ACOG Committee, 2009). The increased risk of developing Type 2 diabetes and its associated comorbidities during later years can be controlled by identifying high risk populations and implementing preventive measures. As the underlying pathophysiology of PCOS is not fully understood and not similar in all cases, the treatment must focus on individual symptoms and on all metabolic consequences and must aim at decreasing future complications (Bargiota and Diamanti-Kandarakis, 2012; Badawy and Elnashar, 2011). More extensive research and understanding of the pathophysiology of PCOS will improve treatment success and overall management of patients. Therefore, the

prudent approach requires emphasis on the modification of lifestyle factors such as diet and exercise to modify risk factors not yet reaching clinical disease. A greater awareness of this aspect would enhance the quality of care by adopting a more holistic life-cycle approach to managing PCOS in women.

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