Achieving a Successful Pregnancy in Women with Polycystic Ovary Syndrome

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KEYWORDS

• Polycystic ovary syndrome (PCOS) • Infertility • Pregnancy

DEFINITION AND EPIDEMIOLOGY OF POLYCYSTIC OVARY SYNDROME

Polycystic ovary syndrome (PCOS), first described by Stein and Leventhal[1] in 1935, is characterized by oligoanovulation, clinical or biochemical hyperandrogenism, and/or polycystic ovaries.[2,3] PCOS is one of the most common endocrinopathies in women of reproductive age, with prevalence estimated between 7% and 8%.[4,5] It is the most common cause of female infertility among reproductive-age women. It is also the leading cause (75%) of anovulatory infertility.[6,7] The prevalence of different phenotypes of PCOS among various populations is affected by ethnic origin, race, and environmental factors.[8]

Currently, there are 3 broadly accepted sets of criteria for diagnosis of PCOS.[2,3] After excluding all other causes of hyperandrogenism and menstrual dysfunction, National Institutes of Health (NIH) criteria (1990) require evidence of hyperandrogenism (clinical or biochemical) and evidence of anovulation or oligo-ovulation. Rotterdam criteria (2003) added the presence of polycystic ovarian morphology as an alternative (2 out of 3 criteria still need to be present for diagnosis of PCOS).[2] The Androgen Excess and PCOS Society criteria (2006) consider polycystic ovarian morphology as an alternative evidence of ovarian dysfunction (**Box 1**).[3] None of these definitions fully addresses the clinical picture of PCOS. For example, none of the sets mentioned earlier includes insulin resistance or increased circulating luteinizing hormone (LH) levels, both common features of PCOS.

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Box 1
Diagnostic criteria for PCOS

NIH (1990)

Anovulation or oligo-ovulation

Clinical and/or biochemical hyperandrogenism

Rotterdam (2003) (2 out of 3)

Anovulation or oligo-ovulation

Clinical and/or biochemical hyperandrogenism

Polycystic ovaries (morphology)

Androgen Excess and PCOS Society (2006)

Ovarian dysfunction

Either anovulation or oligo-ovulation or polycystic ovaries (morphology)

Clinical and/or biochemical hyperandrogenism

PATHOGENESIS AND MANIFESTATIONS OF PCOS

Women with PCOS may present with multiple manifestations, which include cutaneous, reproductive, and metabolic abnormalities. The symptoms are usually peripubertal in onset. The cutaneous manifestations include hirsutism, acne, and male pattern baldness, and are caused by hyperandrogenism. The reproductive manifestations include menstrual dysfunction (secondary amenorrhea, oligomenorrhea), anovulation, infertility, early pregnancy loss, and other complications of pregnancy, which are discussed in detailed later. Metabolic and endocrine manifestations include increased circulating levels of total and/or free testosterone, androstenedione, dehydroepiandrosterone sulfate (DHEAS); decreased sex hormone-binding globulin (SHBG); increased insulin levels; and increased LH/follicle-stimulating hormone (FSH) ratio.

Hyperandrogenism results from abnormalities at all levels of the hypothalamic-pituitary-ovarian axis. The increased frequency and amplitude of LH pulses in PCOS seems to result from an increased frequency of hypothalamic gonadotropin-releasing hormone (GnRH) pulses.[8] The increased LH secretion stimulates theca cells to increase production of androgens. The hyperandrogenic milieu alters the intrafollicular microenvironment, leading to aberrant folliculogenesis.[9]

Obesity, insulin resistance, and hyperinsulinemia are commonly present in PCOS. Approximately 40% to 50% of women with PCOS are overweight,[4] and a history of weight gain frequently precedes the onset of clinical manifestations of this syndrome. Obese subjects with PCOS tend to have more severe reproductive abnormalities and may be resistant to treatment.

In adolescent and young women, the age of onset of obesity and onset of menstrual irregularities are significantly correlated.[10] A large study conducted in the United Kingdom, which included 5800 women, showed that obesity in childhood and in the early 20s increased the risk of menstrual abnormalities.[11] In the Nurses' Health Study, the risk of anovulatory infertility increased in women with higher body mass indices (BMI).[12]

Hyperinsulinemia is present in about 80% of obese women with PCOS and in approximately 30% to 40% of those with normal weight.[13] Overall, 20% to 50% of women with PCOS have insulin resistance and approximately 10 % of women with PCOS develop type 2 diabetes by 40 years of age.[14–16]