PCO and infertility

Dr soheila arefi

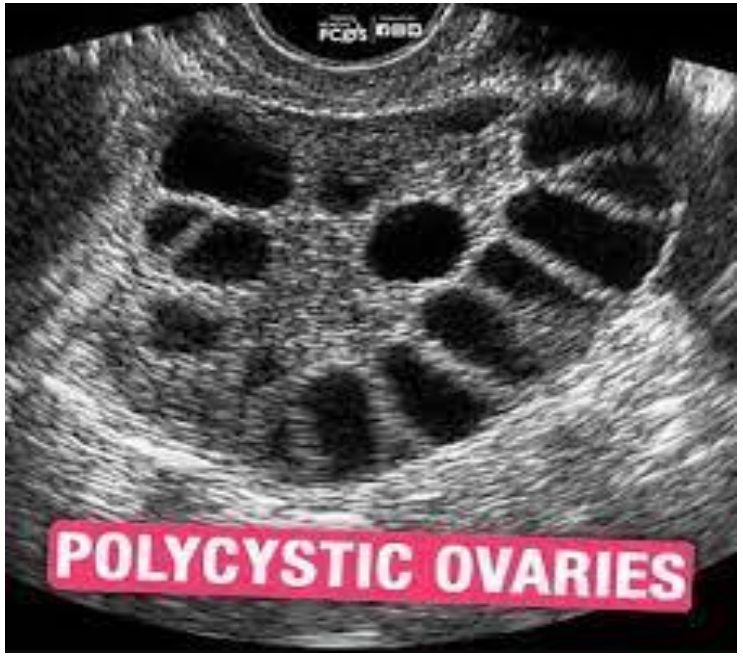
Associated prof.

Avicenna Research Center

- The World Health Organization criteria for classification of anovulation include the determination of oligomenorrhea(menstrual cycle >35 days) or amenorrea(menstrual cycle >6 months) in combination with concentration of prolactin, follicle stimulating hormone(FSH) and estradiol(E2). The patients are classified as WHO1 (15%)—hypo-gonadotropic, hypo-estrogenic, WHO2 (80%)—normo-gonadotropic, normo-estrogenic, and WHO3 (5%)—hyper-gonadotropic, hypo-estrogenic.

- The vast majority of anovulation patients belong to the WHO2 group , as PCOs and demonstrate very heterogeneous symptoms ranging from anovulation, obesity, biochemical or clinical hyperandrogenism and insulin resistance.

- Polycystic Ovary Syndrome (PCOS) is the most common cause of chorionic anovulation and anovulatory infertility .
- PCOS is mentioned as a common endocrinopathy in women who are at reproductive age due to some disturbance in the pattern of pulsatile gonadotrophinreleasing hormone (GnRH) secretion and it is associated with metabolic disorder and reproductive dysfunction.



Wood et al., 2007

- Initial workup in women presenting with oligo/anovulation may include the assessment of serum FSH and E_2 levels to exclude hypogonadotropic hypogonadism (i.e., central origin of ovarian dysfunction) or premature ovarian failure characterized by low E_2 and high FSH concentrations, according to World Health Organization (WHO) classification .

- PCOS is part of the spectrum of normogonadotropic normoestrogenic anovulation (WHO 2) . It should be emphasized, however, that serum LH concentrations are frequently elevated in these patients, routine measurement of PRL in the evaluation of hyperandrogenic patients should be performed to exclude hyperprolactinemia, because many hyperandrogenic patients may have PRL levels in the upper normal limit or slightly above normal.

- The Rotterdam Criteria considers the antral follicle count (AFC) on ultrasound as one of the diagnostic criteria and the serum AMH level could be useful for diagnosis of PCOS.
- The combination of AMH levels (cutoff value = 3.8 ng/mL) and anovulation(oligomenorrhea, infertility, and dysfunctional uterine bleeding) with the presence of hyperandrogenism (hirsutism and acne) was found to have 73% sensitivity and 99% specificity for diagnosing PCOS .

- PCOS is characterized by anovulation due to a developmental defect of follicles beyond 10 mm in size. The clinical manifestations, including infertility, are related to the hypersecretion of LH (70%) present in women with hyperandrogenism anovulatory women, (the ratio of LH/FSH ratio and high increase in ovarian androgen production). Most of the cycles are anovulatory, making it essential to induce ovulation.

- PCOS is commonly associated with insulin resistance, obesity , hyperinsulinemia, components of the Metabolic Syndrome.

March et al., 2010

Hyperinsulinemia plays a prominent role in the development of some phenotypic features of PCOS and, together with β cell dysfunction, increases the risk of developing other metabolic abnormalities such as type 2 diabetes (T2D), hypertension, dyslipidemia, and cardiovascular diseases.

Bednarska S. 2017

Abnormal metabolic features in women with PCOS

- The following cutoffs were considered for dyslipidemia: high total cholesterol ≥200 mg/dL; TG ≥ 150 mg/dL; LDL-C ≥130 mg/dL; and low HDL-C <40 mg/Dl.
- Diabetes and prediabetes were defined using the American Diabetes Association (ADA) classification : categories of increased risk for diabetes were defined as hemoglobin $A1_c$ [A1C] range of 5.7%–6.4%, FPG range of 100–126 mg/dL, or 2-hour oral glucose tolerance test [OGTT] values of 140–199 mg/dL. Diabetes was diagnosed when FPG was ≥126 mg/dL, 2-hour OGTT values were ≥200 mg/dL, or A1C was ≥6.5%.

- Elevated LH levels (about 95th percentile of the normal) can be observed in approximately 40–60% of PCOS patients which affects oocytes by the early resumption of meiosis and premature oocyte maturation with ovulation of the prematurely mature egg will result in either an inability to be fertilized or a miscarriage if fertilization occurs. Balen *et al.* reported that PCOS had a miscarriage rate of 36% when compared with 24% in women with normal ovaries.

Balen AH *Hum Reprod.* 1995

- Both poor oocyte quality and impaired endometrial receptivity can result in implantation failure in the PCOS population .
- In women with PCOS, the regulatory roles of progesterone and progesterone withdrawal in the endometrium is deficient secondary to oligo-ovulatory or anovulatory cycles . This results in a relatively constant low circulating level of estrogens and endometrial changes comparable to the follicular phase throughout the cycle.

- Changes in the expression of endometrial steroid receptor and coactivators in PCOS patients are associated with reduced endometrial receptivity and enhanced actions of estrogen. The term “endometrial receptivity” was introduced to define the state of the endometrium during the window of implantation.

Implantation and uterine receptivity in PCOs

- Decreased HOXA 10 expression in endometrium
- Inhibition of endometrial decidualization and IGFBP-1 expression in stromal fibroblasts
- Increased levels of Heparan Sulfate levels
- Increased levels of IL-6 and MMP

Conclusion

- PCOs is a complex disease cause infertility, due to metabolic disorder, hyperandrogenism, hyperinsulinemia ,oligo /anovulation ,poor quality oocyte and embryo and reduced endometrial receptivity .

Thanks