

Polycystic Ovary Syndrome (PCOS)

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- Diagnosis

Polycystic ovary syndrome (PCOS) is a heterogeneous complex endocrine disorder, whose aetiology remains yet unknown. Key features include menstrual cycle disturbances, hyperandrogenism (raised Free Androgen Index) and obesity (BMI \geq 30 kg/m²). The recognition of characteristic ovarian ultrasound features together with clinical symptoms of oligomenorrhoea, hyperandrogenism, infertility and/or obesity, and altered LH:FSH ratio have been the preferred approaches to diagnose the syndrome in routine clinical practice. Screening for insulin resistance (IR) in women with PCOS is not necessary as IR is not a diagnostic test or prognostic factor.

The ultrasonographic features of polycystic ovaries have to be well distinguished from those typical of other conditions as multicystic ovaries. By and large, multicystic ovaries are often encountered in different physiological and pathological conditions such as normal, mid- and precocious puberty, follicular phase in adult women, hypothalamic anovulation and hyperprolactinaemia. Polycystic ovarian morphology differs from that of normal and multicystic ovaries in that is larger, contains twice as many developing follicles measuring 2-8mm in diameter, mainly arranged peripherally around a dense core of stroma.

The Rotterdam 2003 ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group refined the diagnostic criteria for PCOS, placing great emphasis on ultrasound features (Table 1). In particular, the morphology of the polycystic ovary has been redefined as the presence of 12 or more small follicles in each ovary measuring 2-9mm in diameter, and/or increased ovarian volume more than 10mL (Figure 1). The follicle distribution should be omitted as well as the increase in stromal echogenicity and volume. If there is a follicle greater than 10mm in diameter or a corpus luteum,

the ultrasound should be repeated during the next cycle. The presence of a single polycystic ovary is sufficient to make a diagnosis, provided the woman has other symptoms or signs of the syndrome.

The ultrasonographic features of polycystic ovary have been found in the order of 20% in the general population, while a four-fold increase has been recorded in women with anovulation and idiopathic hirsutism.

Table 1. ESHRE/ASRM-Sponsored Consensus Workshop: PCOS diagnostic criteria (2 out of 3).

- **Oligo- and/or anovulation**
- **Clinical and/or biochemical features of hyperandrogenism**
- **Morphology of polycystic ovaries and exclusion of other aetiologies**

Figure 1. Transvaginal 2D ultrasound appearance of polycystic ovary.



Polycystic Ovary Syndrome (PCOS) - Fertility Treatment

- Education and counselling

- If BMI ≥ 35 kg/m²

regular physical exercise (4-5 times per week)
controlled hypocaloric diet (1200-1400 kcal/day)
Orlistat (120mg TDS)
refer to tertiary care for bariatric surgery

- If BMI $\geq 30 < 35$ kg/m²

regular physical exercise (4-5 times per week)
controlled hypocaloric diet (1200-1400 kcal/day)
Orlistat (120mg TDS)

- If BMI < 30 kg/m²

Metformin (1,5-2,5g daily) for 6 months
Metformin (1,5-2,5g daily) + Clomifene Citrate (50-150mg day 2-6) for 6-12 months
refer for laparoscopic ovarian drilling (LOD)
refer to tertiary care for ovulation induction with gonadotrophins / IVF

Clomifene Citrate (CC)

This compound is a Selective Estrogen Receptor Modulator (SERM) with oestrogen agonist and oestrogen antagonist effects widely used for ovulation induction in women with PCOS. Clomifene is also used empirically in ovulatory women who are trying to conceive.

Ovulation and pregnancy rates after treatment with CC only are 50% and 15%, respectively.

Although very well tolerated by the majority of patients, CC can be responsible for the following side effects:

Bloatedness
Mood swings
Hot flushes
Weight gain
Nausea
Visual disturbances

Treatment with CC may result in multiple pregnancies in up to 10% of cases (cf. 1-2% in spontaneous cycles).

The risk of ovarian hyperstimulation syndrome (OHSS) is minimal, with only a few cases reported worldwide.

Monitoring of CC cycles:

- Day 21 serum progesterone (> 35 nmol/l) – not necessary when prescribed to ovulatory women
- Ultrasound on day 10 of cycle – not necessary
- Urinary β -hCG if no period after 35 days

Metformin

This compound is an insulin-sensitizing agent, extensively used for type-2 diabetes mellitus. Metformin enhances insulin sensitivity in the liver (where it inhibits hepatic glucose production) and in the peripheral tissue (where it induces glucose uptake and utilization into muscle tissue). By increasing insulin sensitivity, Metformin reduces both insulin resistance and hyperinsulinaemia, and does not cause episodes of hypoglycaemia.

Metformin may cause gastro-intestinal side effects. In order to minimise them it is recommended to increase the dose gradually and take it always with food. In cases where high-dose Metformin ($\geq 2\text{g}$ daily) is prescribed for more than 12 months, it is appropriate to monitor the renal function.

Metformin alone has modest beneficial effect in restoring ovulatory function in non-obese patients only. In normal weight patients Metformin is more effective than Clomifene alone in increasing pregnancy rates and reducing miscarriage rates.

Metformin in IVF:

- does not improve response to stimulation
- improves pregnancy rates (in women with BMI $< 28 \text{ kg/m}^2$)
- reduces the risk of OHSS

There is no evidence that Metformin is teratogenic. Studies in the literature have shown no increased risk for congenital abnormalities.

Treatment with Metformin when continued during pregnancy:

- may reduce the risk of spontaneous miscarriage
- may reduce the risk of gestational diabetes, fetal macrosomia and pre-eclampsia