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REVIEW ARTICLE

REVIEW OF POLYCYSTIC OVARIAN DISEASES

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ABSTRACT

Polycystic ovarian syndrome or Polycystic ovarian disease (PCOS or PCOD) in humans is also known as the Stein-Leventhal syndrome. It is a hormonal endocrine disorder of child bearing age recognised as the primary cause of infertility. PCOS is characterised by multiple small ovarian cysts less than 1cm, LH is raised and LH/FSH ratio is ≥2. Endocrine and reproductive symptoms of PCOS are hyperandrogenism (Hirsutism, acne and alopecia), irregular menstrual cycles and sub - fertility. The diagnosis of PCOS depends on establishing key features while ruling out other hyperandrogenic or oligo-ovulatory disorders. Polycystic ovarian disease is a serious disorder in women in which are in fact small undeveloped follicles. Over time there is thickening and fibrosis of the ovarian casing which prevents any follicles which do ripen from being released. PCOD is associated with anovulation and menstrual irregularities, infertility and insulin resistance. As the condition progresses it may become associated with dysfunctional uterine bleeding, obesity, Type 2 diabetes, endometrial cancer, high cholesterol and cardiovascular disease.

INTRODUCTION

Polycystic ovarian syndrome or Polycystic ovarian disease (PCOS or PCOD) in humans is also known as the Stein - Leventhal syndrome. It is a hormonal endocrine disorder of child bearing age recognized as the primary cause of infertility. Polycystic ovarian disease is a heterogenous, multisystem endocrinopathy in women of reproductive age with the ovarian expression of various metabolic disturbances and a wide spectrum of clinical features such as obesity, menstrual abnormalities and hyperandrogenism. Women (5% - 10%) of reproductive age are affected by PCOD[1-5].

Long term consequences include increased risk of endometrial cancer, type 2 diabetes mellitus, dyslipidemia, hypertension and cardiovascular disorders. The etiology of PCOD is not clearly understood, but lipid imbalance, oxidative stress, insulin resistance and genetics are some of the contributing factors. PCOD is frequently diagnosed by gynaecologists and it is therefore important that there is a good understanding of the long-term implications of the diagnosis in order to offer a holistic approach to the disorder. PCOD is characterized by multiple small ovarian cysts less than 1cm, LH is raised and LH/FSH ratio is ≥2. Current incidence of PCOS (5-6%) is fast increasing lately due to change in lifestyle and stress. Amongst infertile women, about 20% infertility is attributed to anovulation caused by PCOD[6-11].

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Fig 1 Normal Ovary and Polycystic Ovary

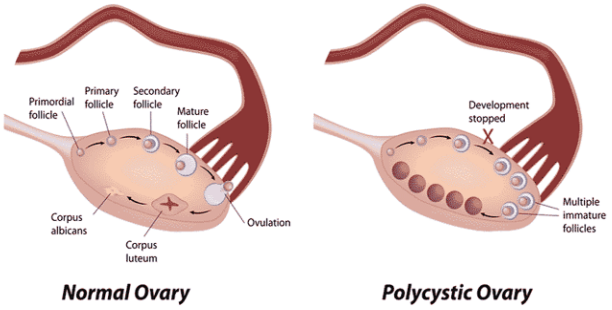

Fig 2 Pathological difference between Normal Ovary and Polycystic Ovarian Disease

Symptoms

Common symptoms, signs & metabolic abnormalities of PCOD [13]

Not all women with PCOD share the same symptoms

1. Oligomenorrhea or amenorrhea, and / or irregular bleeding.
2. Male pattern baldness or thinning of scalp hair, Hirsutism involving face, chest, stomach, back, thumbs or toes.
3. Acne vulgaris – moderate to severe (treatment resistant / cystic).
4. Acanthesis nigricans (patches of thickened, dark brown or black skin) on the neck, arms, breasts or thighs.
5. Skin tags in the armpits or neck area.
6. Depression.
7. Sleep apnea syndrome.
8. Overweight or obesity, usually central.
9. Insulin resistance glucose intolerance and type II diabetes.
10. Hyperlipidemia.
11. Nonalcoholic fatty liver disease.
12. High blood pressure.
13. Anovulation and infertility.
14. High risk of coronary artery disease.
15. Prothombotic state.

Fig 3 Symptoms of PCOD

Causes

While exact cause of PCOD is unknown, doctors believe that hormonal imbalances and genetics play a role. Women are more likely to develop PCOD if their mother or sister also has the condition. Over production of the hormone androgen may be another contributing factor. Androgen is a male sex hormone that women's bodies also produce. Women with PCOD often produce higher-than-normal levels of androgen. This can affect the development and release of eggs during ovulation. Excess insulin (a hormone that helps convert sugars and starches into energy) may cause high androgen levels[18].

Pathology

The ovaries are enlarged. Ovarian volume is increased ≥10 cm^3. Stroma is increased. The capsule is thickened and pearly with in color. Presences of multiple (≥12) follicular cysts measuring about 2 – 9 mm in diameter are found crowded around the cortex[18,19].

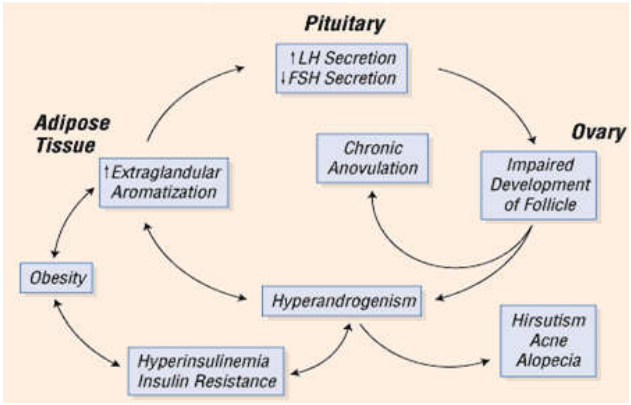

Fig. 4 Pathophysiological changes of PCOD

MORPHOLOGY [18]

The ovaries are usually twice normal size and have a smooth, grey-white outer cortex studded with subcortical cysts 0.5 to 1.5 cm in diameter. On histologic examination, there is a thickened fibrotic superficial cortex beneath which are innumerable follicle cysts associated with hyperplasia of the theca interna (follicular hyperthecosis), Corpora lutea are frequently but not invariably absent.

Clinical Features [18-22]

The pathogenesis appears to be initiated in utero or early adolescents period. Early adrenarche in the form of early pubertal hair and early menarche is observed in a few girls. Menstruation for a couple of years may be normal, but clinical features of PCOD develop early with Oligomenorrhoea (87%) or with a short period of am enorrhoea (26%) followed by prolonged or heavy periods (a common compliant in a majority of cases). Dysmenorrhoea is absent.

In the reproductive years, infertility accounts for about 20% cases. This is due to anovulatory cycles. During pregnancy, if the women conceives, carbohydrate intolerance, diabetes and hypertension may develop. Pregnancy loss occurs in 20-30%. Hyperandrogenism appears in the form of acne (30%) and hirsutism. Facial hair appears over the upper lip, chin, breasts and thighs. Baldness is sometimes noted, but virilism does not develop.

Family history of diabetes and hypertension should be asked. Excessive exercise, history of tuberculosis and thyroid are important in menstrual disorder.

Table 1 Features of Polycystic Ovarian Disease[18]

Mechanism	Manifestations
Pituitary dysfunction	High serum LH High serum prolactin.
Anovulatory Menstrual cycles	Oligomenorrhoea, Secondary amenorrhoea, Cystic ovaries, Infertility.
Androgen excess	Hirsutism, Acne
Obesity	Hyperglycemia, Elevated androgen
Insulin resistance	Dyslipidaemia, Hypertension

Examination

- Obesity, especially waistline. Waist over hip ratio >0.85 is abnormal; 50% women are obese.
- Body mass index between 25 and 30 – overweight; and above 30 – obesity.

- Thyroid enlargement.
- Hirsutism and acne.
- Hyperinsulinaemia which may manifest as acanthosis nigra (5%) over the nape of the neck, axilla and below the breasts; 75% obese women reveal hyperinsulinaemia.
- Blood pressure in obese women.

Pelvic findings are normal, and it is not common to palpate the enlarged ovaries.

For the diagnosis of PCOD, the Rotterdam criteria (2003) suggest that at least two out of three criteria should be present. These criteria are:

- Oligo / Amenorrhoea, Anovulation, Infertility
- Hirsutism – Acne
- Ultrasound findings[10].

Diagnosis [10,18-23]

The diagnosis of PCOD is traditionally made on clinical history and endocrine assessment and there is now an ongoing discussion on the merits of classifying women with the disorders on the basis of endocrine and metabolic criteria versus ovarian Ultrasound based criteria. In many cases, PCOD may be identified solely on the ultrasonographic morphology of the ovaries, however the metabolic disorder may be present in a women with normal-appearing ovaries, and women with ovaries profoundly suggestive of PCOD on ultrasound examination may appear to be phenotypically normal.

There is no specific test for PCOD but your doctor will consider your symptoms and usually complete a physical examination, blood tests and a transvaginal ultrasound.

Physical examination

The doctor will ask numerous questions about your menstrual cycle, symptoms, weight and examine you for physical signs of PCOD, e.g. – acne, excess hair growth and darkened skin.

Blood tests

Blood may be tested for high cholesterol, blood sugar levels (insulin resistance) and for changes in LH (luteinizing hormone) or FSH (follicle stimulating hormone).

Transvaginal ultrasound

A long term slender probe is inserted into the vagina to determine the presence of ovarian cysts or enlarged ovaries and also to examine the reproductive organs or any irregularities. If would prefer not to have a vaginal scan, the doctor may conduct an ultrasound of abdomen done externally while you have a full bladder.

Investigations

Ultrasound is Diagnostic of PCOD

- It confirms the enlarged ovaries, their size and increased stroma. Ovarian volume will be more than 10 mm.
- It shows 12 or more small follicles each of 2-9 mm in size placed peripherally.
- It rules out ovarian tumor.
- It shows endometrial hyperplasia if present.
- Hormonal study mentioned earlier is not performed routinely, but specific hormonal studies are undertaken in a women as and when required. All hormonal studies are not needed as a routine.
- Thyroid function tests in obese woman.
- Laproscopy is reserved for therapeutic purpose, now that the diagnosis can be confirm ultrasound findings. Laproscopy reveals enlarged bilateral ovarian cysts [15-18].

Pharmacotherapy

This includes many agents which may be beneficial in addressing the individual components; however the most popular theraphy now a day is insulin sensitizers, as this is

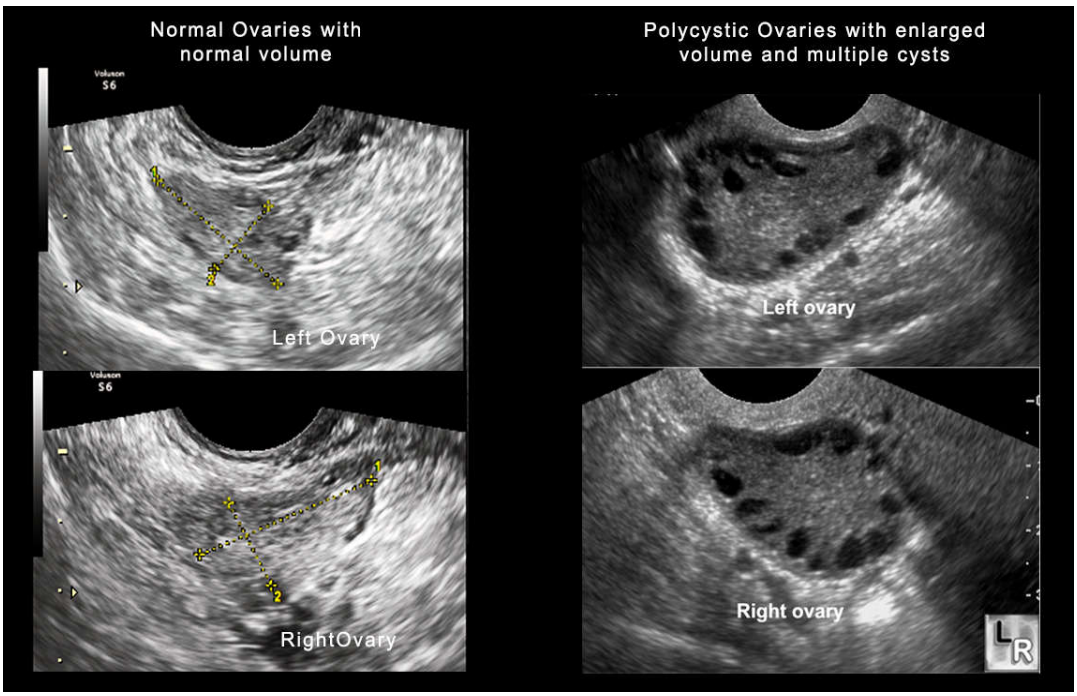

Fig 5 Ultrasound examination of PCOD

supposed to break the root cause of syndrome, the insulin resistance[10,18].

Insulin sensitizers

Metformin

A biguanide that primarily inhibits hepatic gluconeogenesis and lipogenesis and also enhances peripheral glucose uptake, at doses of 1000 – 2500 mg daily, appears valuable in increasing menstrual cyclicity and pregnancy rate. Metformin is preferred given its long history of safe use in PCOD.

Thiazolidinediones are associated with weight gain, fluid retention and heart failure.

Clomiphene citrate

This is an oral oestrogen antagonist that raises circulating concentrations of FSH and induces follicular ultrasound examination and luteal progesterone level. Combination of clomiphene citrate and met form in has been used successfully in a cubset for ovulation induction. Clomiphene with dexamethasone improves fertility rate.

Gonadotrophin treatment

Patients start on low dose recombinant FSH administered subcutaneously. Human chronic gonadotrophin is given when one follicle reaches 16 – 20 mm in size, multiple gonadotrophin cycles may be required to achieve pregnancy.

In – vitro fertilization

Ovulation induction by a skilled reproductive endocrinologist is preferable to *in – vitro* fertilization because of the risks of hyper – stimulation and multiparity with the latter procedures. As clomiphene citrate rapidly blocks steroid negative feedback with 10% multiparity, whereas metformin gradually reduces hyperinsulinemia with low multiparity. Clomiphene citrate may be preferable when time to conceive is essential.

Surgical treatment

Ovarian wedge resection is the surgical removal of part of an ovary. This is done to help regulate menstrual cycles and start normal ovulation. It is rarely used now because of the possibility of damaging the ovary and creating scar tissue.

Laproscopic ovarian drilling is a surgical treatment that can trigger ovulation in women who have PCOD and who have not responded to weight loss and fertility medicine. Electrocautery or a laser is used to destroy portions of the ovaries[23-26].

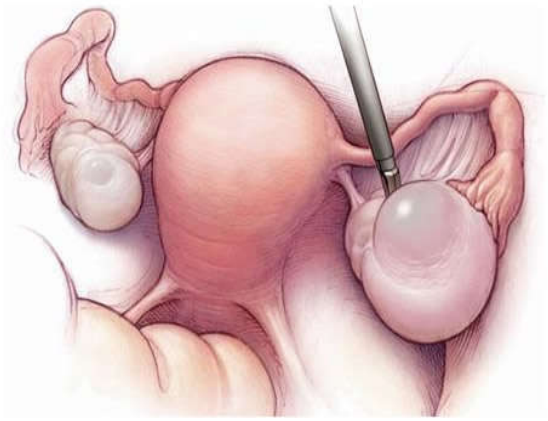

Fig. 6 Ovarian drilling

Risk Factors of PCOD

Cardiovascular Disease

They should hence be regularly monitored and advised to consume less fat and cholesterol. PCOD is characterized by endothelial dysfunction and resistance to the vasodilating action of insulin. An increased risk of myocardial infarction in PCOD women than age – matched controls has also been reported.

Obesity

Obesity is also a feature observed and estimated to effects 50% of PCOD women, classically presented in patients with upper body obesity which has been associated with menstrual disturbances. It amplifies biochemical and clinical abnormalities of PCOD. Previously obesity was thought to be the cause of PCOD but now understood as a modifier of the condition.

Infertility

Infertility is the complicating feature of PCOD is the effects it has on ovulation and fertility with >75% of women with anovulation infertility and treatment is based upon the patient's characteristics.

Complication of PCOD

Endometrial cancer

Recent interest in the long term risks of PCOD has also focused on its possible associations with endometrial cancer. Prolonged anovulation which characterizes the syndrome is considered to be the main mechanism responsible for continual unopposed secretion of estrogens and consequent increased risk of endometrial carcinoma. The known factors which increase the risk of developing endometrial cancer are obesity, long term use of unopposed oestrogens, nulliparity, infertility, hypertension and diabetes.

Complications in pregnancy

Women with PCOD have a greater risk of complications viz. Gestational diabetes, pre – eclampsia, pre – term labor, small for gestational age, pregnancy induced hypertension, spontaneous abortions.

Sleep Apnoea

Women with PCOD have increased Sleep Disordered Breathing (SDB) and daytime sleepiness. Depression there was a higher prevalence of depression in PCOD patients associated with higher body mass index and greater insulin resistance.

CONCLUSION

Polycystic Ovarian Disease is one of the most common female endocrine disorders which may leads to infertility. In this review to thoroughly understand these aspects of Polycystic Ovarian Disease, the causes, symptoms pathology, morphology, treatments and complications were explored. The review on all of these aspects of PCOD will inform the public about how PCOD can affect them and their loved ones. From this newly knowledge, individuals may be able to protect themselves from some of the negative consequences associated with PCOD.

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