

AN OVERVIEW OF PCOD/PCOS

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Article Received on 27/09/2022

Article Revised on 16/10/2022

Article Accepted on 06/11/2022

ABSTRACT

Polycystic ovary syndrome (pcos) is a prevalent disorder in reproductive aged women. pcos is characterized by anovulation, hyperandrogenism, polycystic ovaries. A diagnosis of pcos includes higher risk for infertility, cardiovascular diseases and type 2 diabetes. There are differing treatments for pcos ranging from lifestyle modifications to invitro fertilisation.

KEYWORDS: polycystic ovaries, Cysts, hyperandrogenism, invitro fertilisation, insulin resistance, obesity, diabetes.

Overview

PCOD - condition where ovaries produce immature eggs.
PCOS - metabolic disorder more severe form of PCOD.

PCOS/PCOD is a hormonal disorder which is common among women of reproductive age (14-44 years) which causes enlarged ovaries with small cysts on the edges, may have infrequent (or) prolonged menstrual periods. The preliminary cause of PCOS is due to excess release of male hormones (androgen) in female. The exact cause

of PCOS is unknown, but may involve a combination of genetic and environmental factors. It is one of the most common metabolic and reproductive disorder in women of reproductive age. Women having PCOS have symptoms associated with menstrual dysfunction and excess androgen which impacts the quality of life. psychological disorder. PCOS may increase the risk of obesity, insulin resistance, cardiovascular diseases, endometrial cancer and psychological disorders.^[1]

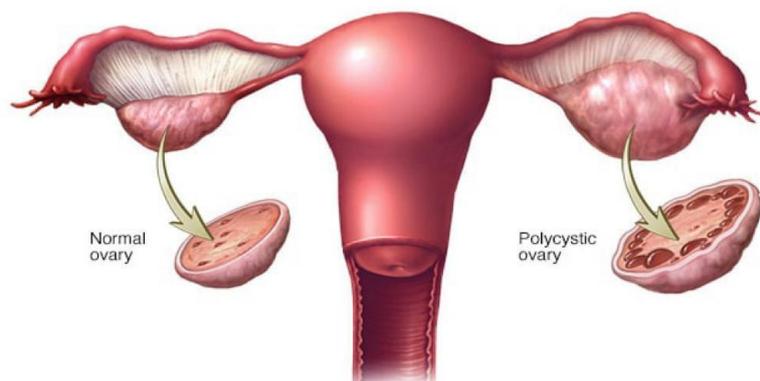


Figure n:(1) Representation of PCOS.

Ages affected by pcos.

6-13 and 60+ years: rare, whereas 14-60: common age affected by pcos.

Incidence

- PCOS effects 4-20% of women globally.
- 3.7-22.5% PCOS cases in India (1million cases).
- 6-12% of US women of reproductive age are prone to PCOS.

- 2-7.5% of women belonging to China suffering with pcos.
- 6.3% of women in srilanka effected by PCOS.

Etiology

PCOS is a multi-factorial disease and can be described as an oligo genic disorder.^[2]

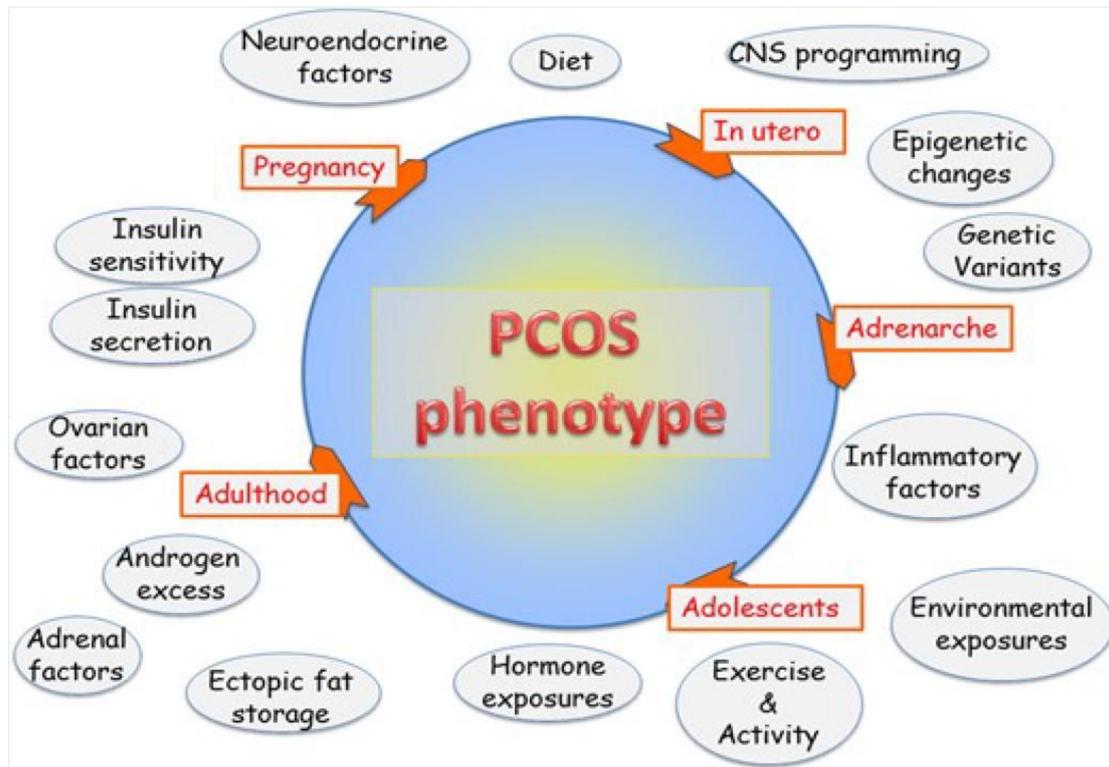


Figure no: (2) Etiology of pcos.

Factors causing PCOS include

1) HIGH LEVELS OF ANDROGEN

- Increase in the levels of androgen prevents the ovaries from releasing the eggs which inhibits the ovulation, which in turn leads to irregular menstruation.
- High androgen levels also cause acne and excess hair growth in women.

2) INSULIN RESISTANCE

- Increased insulin levels in the body cause the ovaries to release male hormone (androgens). Increased male hormone, which leads to, suppress ovulation and contribute to other symptoms of PCOS.^[3]

3) OBESITY AND CARDIOVASCULAR RISKS

- The increased abnormal fat and insulin resistance leads to risk of type 2 diabetes and cardiovascular diseases. Obesity increases some factors such as HYPERANDROGENISM, HIRSUTISM, INFERTILITY AND PREGNANCY COMPLICATIONS.

4) HEREDITY

- Many researchers suggest that the PCOS is linked to certain genes which are heritable.

Pathophysiology

Earlier, intrauterine androgen had been thought to be main cause of the development of the disease. Upon recent studies it is neither an association between excessive prenatal androgen exposure nor elevation in androgen levels in cord blood of females born to mothers with PCOS/ PCOD.

- The primary cause of PCOD affects the hypothalamic pituitary axis, insulin secretion and ovarian function.
- Genetics, obesity, sedentary lifestyle and intrauterine androgen exposure and few other factors leads to the excess release of gonadotropin releasing hormone (GNRH) in progesterone from the hypothalamus leads to hyper-secretion of luteinising hormone by the pituitary-gland.

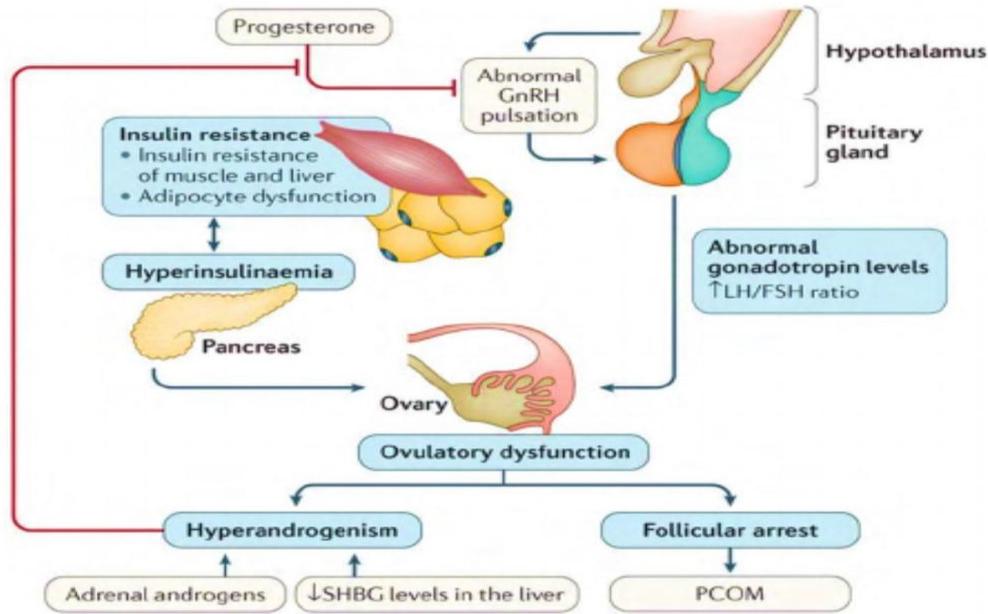


Figure no (3): Pathophysiology of PCOS.

The excess release of luteinizing hormone induces ovaries dysfunction and hyper androgens. Intrinsic ovarian factors such as altered steroidogenesis and factors external to ovary such as hyper-insulinemia contribute excess ovarian androgen production.^[4] The excess release of androgen leads to arrest in antral follicle development which may lead to an-ovulation or formation of polycystic ovaries that leads to disturbed

secretion of luteinizing hormone, is thought to occur early in puberty and is related to disturbed inhibition of GNRH secretion by progesterone leads to unopposed increased in oestrogen. Gradually leads to PCOD and in extreme conditions leads to PCOS. Some studies suggest that PCOS is a primary defect in young girls and who have family history of the disorder. Approximately 25% of patients with PCOS have elevated prolactin levels.

The symptoms and risk factors of pcod include^[7]

Table no: (1)

| SYMPTOMS | RISK FACTORS |
|--|--|
| Menstrual irregularity. | Type2 diabetes. |
| Hyper androgenism. | Psychological disorders. |
| Breakouts like acne, oily skin and dandruff. | Endometrial cancer. |
| Pain in pelvic area. | Abnormal uterine bleeding. |
| Depression and anxiety. | Steato hepatitis (non-alcoholic and liver diseases) |
| Obesity. | Blood pressure increases with increase in insulin levels |
| Infertility. | Coronary heart diseases |
| Sudden weight gain (or) weight loss. | |
| Decreased libido, skin tags. | |
| Sleep apnoea. | |

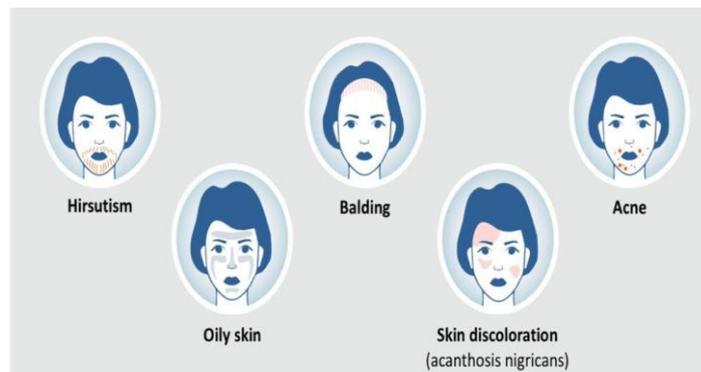


Figure no: (4) Symptoms of PCOS.

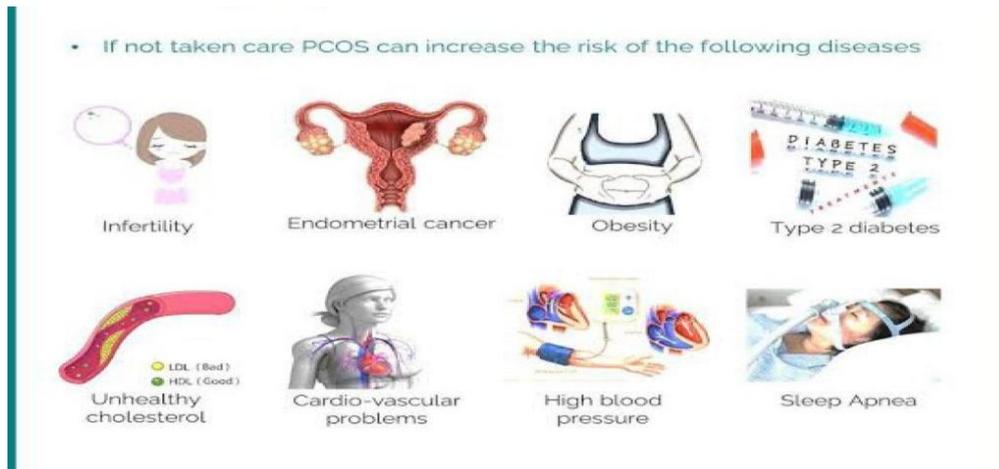


Figure no: (5) Risk factors of PCOS.

Diagnosis

A single diagnostic test is not specific for detecting product a doctor can diagnose a condition through patients' medical history.

The physical examination includes.

1. Pelvic exam

The growth and abnormalities are detected visually and manually by the doctors.

2. Blood test

To measure hormone, cholesterol and glucose levels.

3. Ultrasound scan

The appearance of ovaries and thickness of lining of uterus is checked by ultra sound scan.^[8]

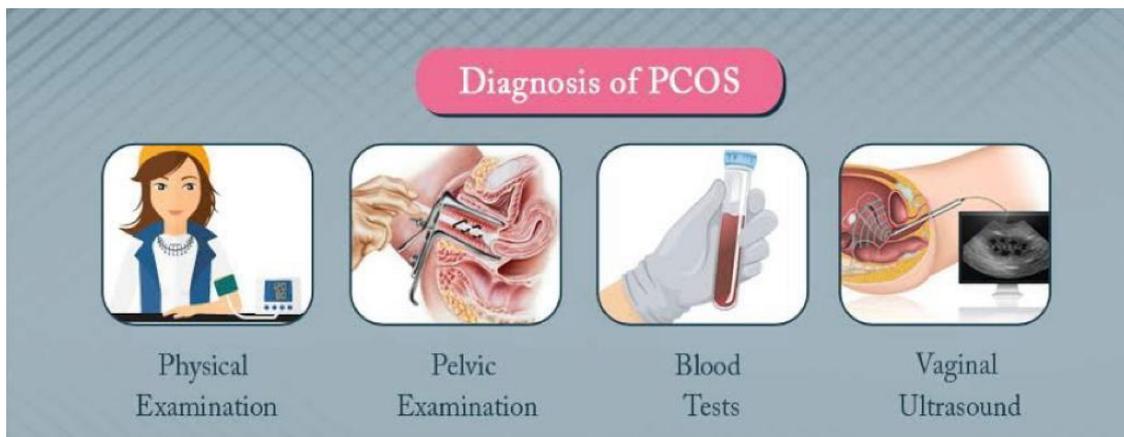


Figure no : (6) Diagnosis of PCOS.

Treatment

The most common complaints of PCOS involves an-ovulation, hirsutism or acne.

A.) Metformin.

- Metformin is a anti diabetic, biguanide drug which is taken orally.
- The earliest studies conducted by Velazquez in 1994 by using Metformin on pcos patients revealed that 35% decrease in insulin area and 31% reduction in insulin area to glucose ratio. It is disclosed that Metformin does not improve insulin resistance instead it improves glucose effectiveness.
- Even though the earlier studies showed contradictory results with respect to Metformin effect it is described as first line treatment for cutaneous demonstration and pregnancy complications in women with pcos.

Mechanism of action

Metformin was the first insulin sensitising drug (ISD) to be used in PCOS to investigate the role of insulin resistance in the pathogenesis of the pcos. Metformin is an antidiabetic drug that increases glucose utilization in insulin-sensitive tissues. As Polycystic Ovary Syndrome (PCOS) and diabetes share some altered parameters-such as abnormal glucose: insulin ratio, altered lipidic metabolism and insulin-resistance syndrome- the use of metformin has become increasingly accepted and widespread in the treatment of PCOS. Currently, metformin is used to induce ovulation and during early pregnancy in PCOS patients, however, a complete knowledge of the metformin action has not been achieved yet. This review describes beyond the classical reproductive action of metformin and explores other benefits of the drug. In a comparison of simvastatin and

metformin in women with pcos total testosterone levels were reduced by 17.1% and 13.6% respectively.^[15]

B.) Antiandrogens

- They act either by competitive inhibition of androgen binding receptors or inhibit 5-alpha reductase enzyme results in decrease of androgen production.
- Oral contraceptive pills can also be added with all anti androgens in sexuality active women because of risk of feminisation of male foetus if pregnancy occurs.
- Spironolactone, flutamide and finasteride are the antiandrogens that work in pcos by decreasing androgen levels, thereby reducing the signs of hirsutism and acne.^[16]

C.) clomiphene

- It is an anti-oestrogen medication taken orally during first phase of menstrual cycle.
- Clomiphene/metformin combination may be tried if individual therapies fail but evidence of improved results is limited^[14]
- This medication combination inexpensive and invasive treatment for patients with pcos.

Surgical approach for pcos

- There are two types of ovarian surgeries to cure pcos
- 1) Laparoscopic ovarian surgery
- 2) Ovarian block resection

Laparoscopic ovarian surgery

- In the recent years there is an established research in the surgical procedures because of increasing field of operative laparoscopy. electrofulguration is being tried by various workers.^[5]
- It involves the use of simple mechanical puncture of ovaries, laser treatment, electrofulguration are being tried by different workers.
- Electrofulguration can give an armamentarium of gynaecologist.^[6]

Emerging therapies in pcos

1.)Statins

- The latest treatment option that have been included in the treat protocols of pcos are statins.

Mechanism of action

- They are used in the treatment of pcos as they decrease sex steroids production and improve dyslipidaemia and reduce ovarian androgen production of theca-cells.^[9,10]
- In *in vitro* experiments on human theca –interstitial cells, statins have been shown to inhibit proliferation of human theca-interstitial cells irrespective of the availability of cholesterol and independently of leukocytes, both in normal and PCOS ovaries.^[11]
- Mevalonate pathway plays a major role in the function of theca-interstitial cells and modulation of this pathway by statins, may provide both cardiovascular (CV) and ovarian benefits in PCOS.^[12]

2.)Aromatase inhibitors

- They are newly developed drugs used as ovulation inducing agents.

Mechanism of action

- Aromatase inhibitors such as anastrozole and letrozole they inhibit the conversion of testosterone, androstenedione to estradiol and estrone respectively.
- They reduce estrogenic activity which results in the releasing the hypothalamus from negative feed back mechanism and increase the follicle stimulating hormone release.^[13]
- Letrozole has also been proven to be more effective than metformin in terms of live birth rate for WHO Group 2 (including PCOS) anovulatory women.

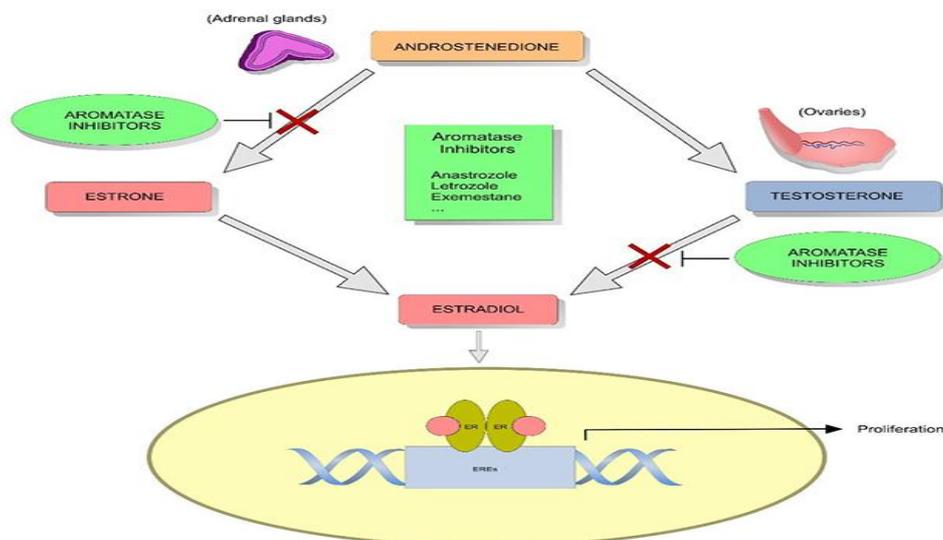


Figure no (8): MOA of Aromatase inhibitors.

Future prospects in the treatment

- Presently, cocs (combined oral pills) are used to treat PCOS as the primary treatment. These include many medicines that improve the ovulation. Combination of medications are used to increase the chances of conception.^[17]
- However, using of this combinational medications leads to severe adverse effects like cardiac pathology, diabetes mellitus and depression.^[18]
- To reduce the risk of this adverse effects some procedures were developed. These procedures

include IVF, IVM fertilisation and laparoscopic drilling. These procedures also involve many no. of secondary diseases.^[19]

- It is now suggested that a team composed of endocrinologist, a physician, gynaecologist and reproductive medical specialist will help the patients suffering from PCOS.
- For the future it is important to develop strategies for the prevention of over weight and obesity in order to improve reproductive and metabolic health.

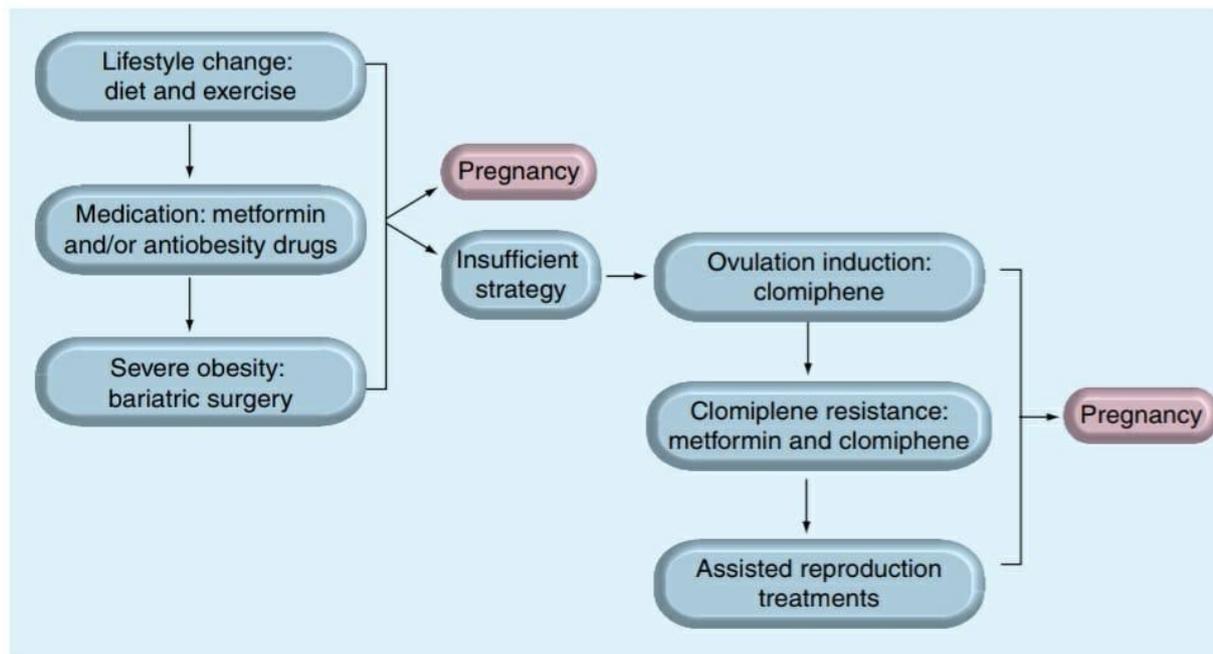


Figure no (9): PCOS in pregnancy.

CONCLUSION

In conclusion, PCOS is becoming a more prevalent disorder among women of reproductive age with lifelong complications. One of the most challenging aspects of this syndrome is it is an ambiguous diagnostic criteria and vast complexity of characteristics. In the future, more research in the genetics and pathophysiology of PCOS is needed to determine preventive risk factors as well as successful treatment modalities for this syndrome.

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