REVIEW ARTICLE

Poly Cystic Ovarian Syndrome: An Updated Review

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Abstract

Polycystic ovarian syndrome(PCOS) is the most common endocrine and inflammatory disorder in women associated with oligo-anovulatory infertility and cardiometabolic disorder. Insulin plays a vital role in PCOS; it is also responsible for regulating the action of ovarian and liver metabolic enzymes and also involved in the production of Androgens. The hyperandrogenism prevalence nearly (70-80%). In PCOS, the target tissue is controlled by sex hormone-binding globulin(SHBG) because this is a type of protein produced by hepatic and tightly bind with testosterone and as well as dihydrotestosterone (DHT) and estradiol.[3] Currently study reported, associated with rs6259 polymorphism with link SHBG level and PCOS in most Indian women, nearly 3-5%. The PCOS cases associated with isolated functional adrenal hyperandrogenism and the remaining case of PCOS maybe lack clinical evidence of steroids secretory dysfunction. Most of the females are obese in PCOS; the treatment approaches of PCOS are towards improving insulin tolerance reduce the level of androgen and maintain the normal menstrual cycle and regulate proper fertility. Nonpharmacological approaches are also helpful, like proper exercise, weight management, and maintain healthy diets. The etiology is still unclear, not clear, and has no cure. Some studies reported dysregulation of the gut microbiome and played the crucial role played in Pathogenesis in PCOS.

Keywords: Hyperandrogenism, SHBG, PCOS, an endocrine disorder, Insulin resistance, menstrual cycle, endometrial hyperplasia, Antiandrogenic.

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Introduction

Now these days Polycystic ovary syndrome most common endocrine and reproductive disorder in women. It is a worldwide prevalence of nearly 10-18% in women.[1] PCOS is a condition characterized by irregular periods and increases the level of Androgens and formation of poly cysts in ovaries.[2] Chronic PCOS leads to cardiovascular problems, diabetes, and endometrial cancer and also disturbed feeling well being. Female infertility also linked with PCOS. On the other way, Endometrial Hyperplasia is a common condition that affects most of the women in all age groups because excessive cellular proliferation leads to increased thickness and volume of endometrial tissue.[3] The Pathogenesis of PCOS is Multifactorial involve interactions between genetic, Environment and mental stress, obesity, and lifestyle. An excessive level of Androgens leads to hyper-insulinemia/insulin resistance[4] a significant prevalence is obesity in PCOS, because, nearly 60% of women being obese. Most of the common feature is ovarian dysfunction associated with excess androgens, which leads to chronic oligo/anovulation and menstrual abnormalities. And excessive androgen also causes dermatological complications like- male pattern baldness, acne, and hirsutism like symptoms. [5] In PCOS, oxidative stress plays a crucial role because increased oxidative stress leads to cell damage and many other complications.

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Because Reactive oxygen species are highly reactive molecules or ion and generate free radicals like H_2O_2 and a hydroxy group, Nitric oxide, Inflammation also play a major role in PCOS because increasing the level of inflammatory mediators.[6] Endometrial hyperplasia is also a significant complication of PCOS because sometimes increase the level of estrogen is a potent inducer of the proliferation of the endometrium.[7] Endometrium hyperplasia also occurs due to mutation of PTEN (Phosphate and tensin homolog) gene.[8] In the current date, 70% of lean females and 90% of overweight diagnosed with PCOS and Atherogenic dyslipidemia are occurs nearly 70% of individuals and elevated fasting plasma TG, Cholesterol, and as well as low-density lipoproteins cholesterol

Table 1: Symptoms associated with PCOS

USUAL SYMPTOMS OF PCOS	*MENACE OF FUTURE LIFE*
The menstrual cycle is disturbed, heavy bleeding, or some time absence of bleeding.	Due to absence or fewer periods (3-4 periods in a year) lead to a risk of endometrial cancer.
Difficulty in getting pregnant or infertility	Sleep apnoea.
Immoderate hair growth on an unwanted area like face, neck, breast, buttock, etc.	Frustration, anxiety.
Obese	Type 2 diabetes.
Excessive loss of hair and thinning of hairs leads to baldness.	Depression
Oily skin or acne. Patches on skin.	High blood pressure and high cholesterol lead to heart disease and stroke.
Headache.	High risk of many metabolic and neurological disorders associated with alteration in hormones.

(LDL-C).[9] The risk of atherosclerosis also increases due to raising TG and bad cholesterol.

Treatment criteria

Currently, the treatment of PCOS is based on complications like-Maintain the menstrual cycle, decrease the level of androgen, infertility treatment, and obesity.[10] Estrogen receptor modulator like-Clomifene is first-line therapy till now.[11] Clomifene directly acts on the hypothalamic-pituitary axis. Another drug, if patient obese and diabetic, then used metformin, it provides a beneficial effect nearly up to 4-6 months. Metformin is well known Antidiabetic biguanide derivatives; it reduces the level of insulin and androgen and maintains the ovulatory cycle and menstrual periods.[12] It's also improved the lipid profile and increase the Antioxidant action in the body. Metformin also acts on Sex hormone-binding globulin (SHBG).[13] In a certain study reported metformin acts as protect against developing endometrial and used as breast, intestinal, and hepatic cancer by inhibiting mTOR. Another pharmacological approach, like oral contraceptives, to avoid pregnancy. The oral contraceptives maintain a rhythm of bleeding and reduce the excess level of androgen and also reduce the risk of endometrial hyperplasia. Nowadays, a physician prescribes combination therapies cyproterone acetate combined with Ethinyl estradiol, and spironolactone or metformin.[14] Another goal of the PCOS patient obese, so physicians guide lifestyle modification and other complications like Androgenic alopecia and acne. In the case of Androgenic alopecia used 5-alpha reductase inhibitors (Finasteride) or Antiandrogenic drugs like (Cyproterone acetate) and for alopecia used topical preparation of minoxidil 2% solution nearly 4-6 months. Isotretinoin is used first-line treatment of acne associated with PCOS.[15] Some of the studies suggest that vitamin-D also helps in PCOS.

Diagnosis

Some major diagnoses have been reported for PCOS. According to the National Institute of Health (NIH), we include clinical/biochemical hyperandrogenism and oligo/amenorrhea anovulation and other criteria polycystic ovarian morphology on ultrasound.[5] In laboratory test includes the identity level of androgen, glucose, TG, and fasting cholesterol. In the pelvic exam, doctors check masses, growth, or abnormalities.

Pathophysiology

In the pathophysiology of PCOS, the synthesis of androgen is increased, which leads to disruption of folliculogenesis and resistance of insulin.[16] These factors are contributing to their role in the pathophysiology of PCOS. The dysfunction of the endocrine system of women resulting in dysfunctioning of metabolism and

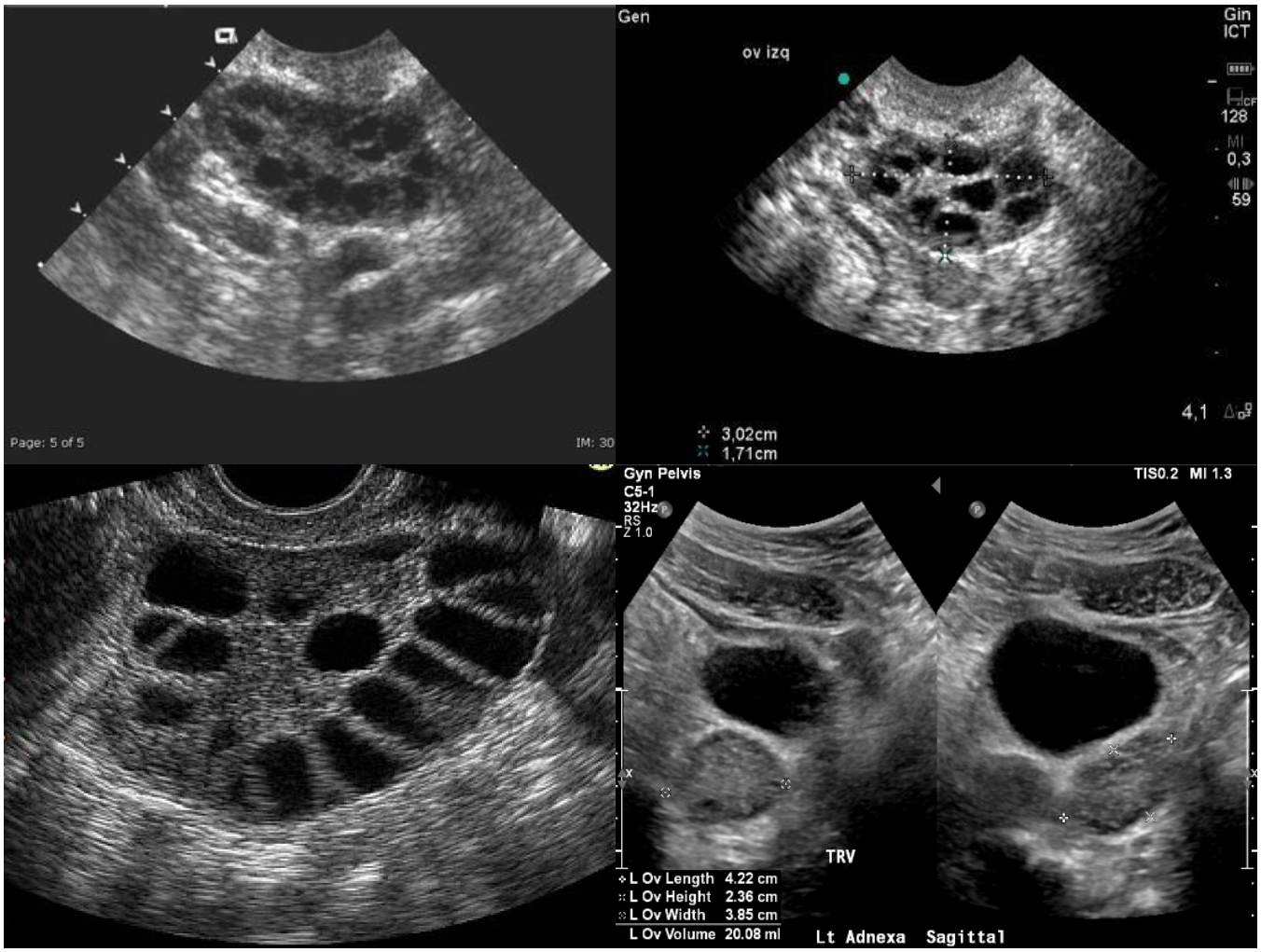

Figure.1

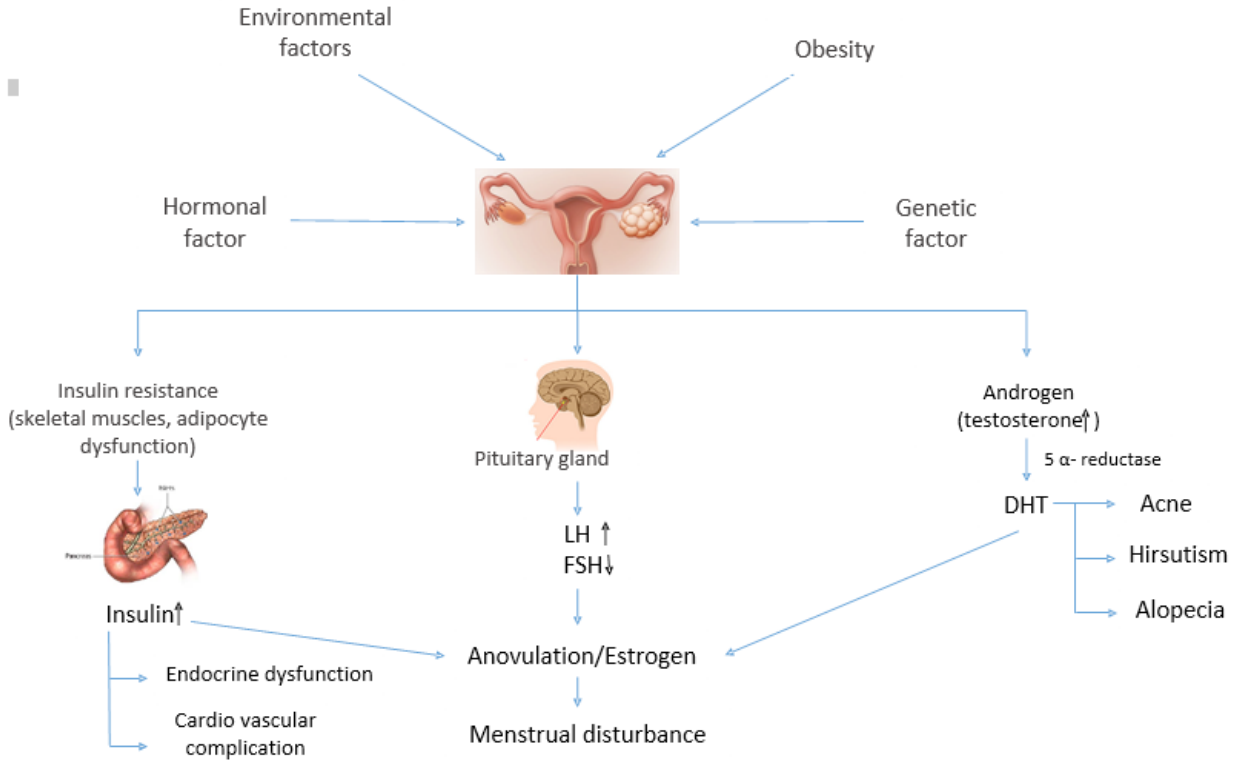

Figure.2

the genetic factors also play a key role in PCOS. 60-80% of PCOS patients with adrenal/ovarian origin due to hyperandrogenism. An inherent steroidogenic defect of theca cells mainly alleges by hyperandrogenism in PCOS. The intrinsic abnormality of the ca steroidogenesis is intensified by the high level of luteinizing hormone (LH) and insulin level.[17] The factor like intraovarian factors and diminish the level of follicle-stimulating hormones (FSH) levels are also contributing their role in PCOS progression. Augmented androgen production is the cause to be an intrinsic steroidogenic defect in PCOS theca cells.[18] In vitro studies shows that the increase the action of the mainly the enzymes that are 17α-hydroxylase\17,20-lyase(CYP17α1), 3-β-HYDROXYSTEROIDS DEHYDROGENASE TYPE ii (HSD3B2)and side-chain cleavage enzyme (CYP11A1) occupy by the increased activity of steroidogenic PCOS theca cells .in the process of androgen synthesis these three enzymes have participated differently, e.g., the first step of steroid biosynthesis where conversion of cholesterol to pregnenolone occurs with the help of CYP11A1 enzyme. Where the rest two enzymes dually exert their action by involving conversion of 17α hydroxypregnenolone and 17α-hydroxyprogesterone to form dehydroepiandrosterone (DHEA) and androstenedione. Altered gonadotrophins are also responsible for the excessive level of androgen synthesis, and the theca cells are directly affected by the LH. The conversion of estrogen from androgen is not carried out due to a decreased level of the FSH by diminished stimulation of aromatase.[19] Insulin is also suggested that one of the major causes of the dysregulation of theca steroidogenesis in PCOS. The androgen synthesis is stimulated in PCOS by the symbiosis of both LH and insulin; due to symbiosis work, the insulin is supposed to the second cause of intermittent follicular maturation disturbed\arrest ovulation in PCOS. Excessive insulin levels also defect the receptor present on granulusa cells. In PCOS, insulin resistance can also be seen in skeletal muscle and adipose tissues, and they directly or indirectly interface with metabolic function.[20]

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