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PREVALANCE OF POLYCYSTIC OVARY SYNDROME IN REPRODUCTIVE-AGED WOMEN

Syed Mohiuddin[1], Nabeela Zufi[1], Dr. Ch Pradeep Kumar [2]
1. Pharm-D, Department of Clinical Pharmacy, Vaageswari College of Pharmacy, Karimnagar, Telangana.
2. Associate Professor, Vaageswari College of Pharmacy, Karimnagar, Telangana.

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Corresponding author*
Syed Mohiuddin, Vaageswari College of Pharmacy, Karimnagar, Telangana.
syedbilaluddin5@gmail.com

ABSTRACT

REVIEW ARTICLE

Polycystic ovary syndrome (PCOS) is one of the most communal endocrine illnesses in women of reproductive age. The clinical and biochemical presentation is heterogeneous, but elevated serum concentrations of androgens are the most consistent biochemical abnormality and may be considered to be the hallmark of the syndrome. Many women with PCOS also have insulin resistance and hyperinsulinemia, which may contribute to the clinical and endocrine abnormality. Obesity, central obesity and insulin resistance are powerfully concerned in its etiology. Dietary weight loss is recommended as the primary treatment approach. Our aim is to control prevalence, etiology of PCOS, diagnosis and its association numerous factors in PCOS patients, so as to encourage young women to treat timely treatment and prevent long term complications.

INTRODUCTION:

1. About the disease

Polycystic ovarian syndrome (PCOS) is a common endocrine condition in women of reproductive age with prevalence estimated at 4–8%(1). Its clinical manifestation comprises variable reproductive and metabolic aberrations. These include menstrual dysfunction, infertility, pregnancy complications, clinical and biochemical hyperandrogenism and an increased prevalence of obesity and abdominal obesity (2). There is also an increase in risk factors for diabetes mellitus and cardiovascular disease including impaired glucose tolerance, hyperlipidemia (decreased plasma high-density lipoprotein cholesterol (HDL-C and increased plasma triglycerides), hypertension, inflammation and endothelial dysfunction (3,4,5) and there is controversial evidence on the presence of gestational diabetes in women with PCOS (6,7).

Insulin resistance and compensatory hyperinsulinemia are present in a high proportion of women with PCOS and play a key aetiological role in PCOS through insulin stimulating thecal cell androgen production (8) and decreasing hepatic sex hormone-binding

globulin (SHBG) production (9), resulting in increased concentrations of total and free androgens. Thus, lean and overweight women with PCOS are generally more insulin resistant than body mass index (BMI) matched control women and insulin resistance in lean women with PCOS is augmented by the presence of insulin resistance associated with obesity (10). Not all women with PCOS exhibit hyperinsulinemia and insulin resistance (11), although insulin-resistant women with PCOS are more severely clinically affected than insulin-sensitive women with PCOS (12).

2. Signs and Symptoms of PCOS

The characteristic demonstration of PCOS usually varies with age, young women mostly complaining of reproductive and psychological problems while older women complaining of metabolic symptoms (13). signs, symptoms, and laboratory values mutual in patients with PCOS. A thorough physical examination, medical history, and laboratory tests should be conducted to reach the appropriate diagnosis(14). In addition, in the one hand, challenging must include an assessment of the metabolic status of the patient, i.e., measurement of her body mass index (BMI), On the further pointer, screening for thyroid disorders thorough assessment of thyroid-stimulating hormone levels is considered important as thyroid disorders are a common cause of menstrual irregularity (15).

2.1 Hyperandrogenism

Puberty is characterized by physiological hyperandrogenism(16). Multiple studies showed that testosterone levels rise during puberty and reach a peak adult level within a few years after menarche. (17-20).

2.2 Menstrual Irregularity

Adolescents often exhibit physiological menstrual irregularities such as oligomenorrhea(21), typically during the first 2 years after menarche, owing to lack of maturation of hypothalamic-hypopituitary-ovarian axis(22). Completed near observation of the menstrual cycle outlines, clinicians have to di□erentiate physiological anovulation associated with puberty from pathological anovulation as a dysfunction identified in PCOS (23,24).

3. Etiology and Pathogenesis

PCOS has been attributed to several causes including modification in lifestyle, diet, and stress. Initially, the ovaries were supposed to be the primary source, that usually the changes in the endocrine pattern. Genetic and familial environment factors (autosomal dominant inherited factors) were later added as etiological factors in the growth of PCOS. The environment factor may function in the utero or in early adolescent life, demonstrating clinically a few years later as PCOS. Familial incidence has been reported. The X-linked dominant mode of inheritance is also involved. Another view held for the incidence of PCOS is enhanced serine phosphorylation unification activity in the ovary (hyper androgen) and reduced insulin reception activity superficially (insulin resistance). Obesity is related to PCOS. The adipose tissue (fat) is considered an endocrine and immunomodulatory organ; it secretes leptin, adiponectin and cytokines which interfere with insulin signaling pathways in the liver and muscle resulting in insulin resistance, and hyperinsulinemia. Endogenous endorphin also stimulates insulin release and may contribute to insulin resistance. Hyperandrogenism and resulting anovulation were initially thought to arise primarily in the ovaries. Insulin induces LH to cause thecal hyperplasia and secrete androgens, testosterone and epi-androstenedione which are converted to estrogen in the granulose cells. Epi-androstenedione is converted in the peripheral fat to oestrone. This leads to a rise in estrogen and inhibin levels. These, in turn, cause a high LH surge. While oestrone level increases, the oestradiol level remains normal with the result that the oestrone/oestradiol ratio rises. Hyperandrogenism lowers the level of hepatic sex hormone-binding globulin (SHBG) so that the level of free testosterone rises leading to hirsutism. Androgen also suppresses the growth of the dominant follicle and prevents

apoptosis of smaller follicles which are normally destined to disappear in the late follicular phase. The polycystic ovarian syndrome may set in early adolescent life, but clinically manifest in the reproductive age with long-term implications of diabetes, hypertension, hyperlipidemia, and cardiovascular disease; this cluster of disorders is known as the 'X syndrome' (3).

3.1 Thyroid related to PCOS

In hyperthyroidism, higher levels of sex hormone-binding globulin (SHBG), estradiol (E2), testosterone, androstenedione, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) compared with the euthyroid state were established(25). In addition, hyperthyroidism is associated with irregular menstrual cycles, while ovulation is usually preserved in otherwise healthy women (26). In hypothyroidism, lower levels of SHBG, E2, testosterone, and androstenedione were described. Prolactin levels may be increased due to increased TRH secretion. Levels of LH and FSH were normal (25, 26). Hypothyroidism may be associated with ovarian cyst formation as shown in a case report (27). In gilts, hypothyroidism increased ovarian sensitivity to gonadotropin action and led to marked hypertrophy of ovaries as well as to the formation of multiple follicular cysts (28). Hypothyroidism may cause heavy, irregular menses, breakthrough bleeding, low endometrial thickness, ovulatory dysfunction, and sometimes non-proliferative endometrium due to anovulation(29).

3.2 Effect of obesity on the pathophysiology of PCOS

Obesity may play a pathogenic role in the development of PCOS in susceptible individuals, as well as exacerbating the clinical and metabolic features of the syndrome. Obesity is present in 30–75% of women with the syndrome(30) and has a negative impact. Women who are obese more often have severe hyperandrogenism (hirsutism, menstrual abnormalities, and anovulation) than normal-weight women with PCOS.

The distribution of body fat also has an important impact on the pathophysiology of PCOS. Studies have shown that 50–60% of women with PCOS have an abdominal distribution of body fat (central obesity), regardless of their body mass index (BMI) (31,32).

In women with PCOS, intravisceral adipocytes behave in an abnormal way in terms of their effects on the metabolic and hormonal profile. This abnormal adipocyte behavior is associated with defective insulin activity, leading to impaired glucose tolerance, hyperinsulinemia and insulin resistance.

There is no defect in the process by which insulin binds to its receptor in women with PCOS. Instead, visceral adipocytes are believed to express defects in insulin intracellular signaling. The β-subunits of the insulin receptor increase serine phosphorylation, which inhibits the intracellular transmission of the insulin message in the adipocytes, and decreases tyrosine phosphorylation. This defect is, in turn, translated into the decreased activity of the PI3K (phosphoinositide-3 kinase) enzyme, which is the key enzyme for the recruitment of GLUT-4 (glucose transporter-4). GLUT-4 is responsible for the insulin-dependent glucose uptake by the cells, so the reduction in its activity can, therefore, result in decreased cellular glucose uptake with an increased risk of glucose intolerance and type 2 diabetes(33).

4. Adolescence

Acne is common during the adolescent years, whether or not PCOS is present, whereas hirsutism—associated with PCOS—typically develops over time. Hyperandrogenemia may be a more consistent marker for PCOS during the teenage years (34). As many as 85% of menstrual cycles are anovulatory during the first year after menarche, while up to 59% are still anovulatory during the third year following menarche (35). In one study, persisting oligomenorrhea was not predicted by increased androgens, polycystic ovaries on ultrasound or increased serum LH levels(36). Only around

40% of adolescent women with menstrual irregularity have polycystic ovaries on ultrasound(37).

5. Contraception

Women with PCOS who do not desire pregnancy need contraception. No contraceptive methods are contraindicated in PCOS. Some of the features associated with PCOS [obesity, insulin resistance (IR), etc.] may represent a relative contraindication to the use of combined OCPs. Cycle control is usually achieved by the use of OCPs in women with PCOS. OCPs suppress LH secretion and lead to a decrease in ovarian androgen production. The estrogenic component increases the levels of SHBG, which, in turn, results in a decrease in circulating free T levels. The progestin in the pill can compete for 5a-reductase at the level of the androgen receptor. Oral contraception also decreases adrenal androgen production by a mechanism yet unclear, possibly due to a decrease in adrenocorticotropin hormone production (38).

6. COMPLICATIONS

a. Reproductive aged women in PCOS

The oligo- or anovulation associated with polycystic ovary syndrome can result in reduced fertility. The prolonged absence of ovulation also can result in continuous endometrial stimulation by estrogen, unopposed by progesterone. Thus, women have an increased risk of endometrial hyperplasia and possibly endometrial cancer. Regulating menstrual cycles to prevent endometrial hyperplasia is one of the major treatment goals. It is important to note that many of the treatments that improve insulin sensitivity, such as weight loss, metformin, and thiazolidinediones, may also increase the frequency of ovulation and, thus, improve fertility.

b. Metabolic Women

With polycystic ovary syndrome are at a markedly increased risk of type 2 diabetes (39). Additionally, they may have an increased risk of gestational diabetes. Polycystic ovary syndrome is associated with several other metabolic complications including central obesity, hypertension, dyslipidemia, nonalcoholic fatty liver disease, and obstructive sleep apnea. Surrogate markers for cardiovascular diseases, such as carotid artery intima-media thickness, coronary artery calcification, and C-reactive protein are also abnormal.

c. Psychological Issues

Although research on psychological issues is limited, small studies have found that women with polycystic ovary syndrome have high prevalence rates of depression and reductions in health-related quality of life and sexual satisfaction. In addition, eating disorders may be more prevalent(40).

7. DIAGNOSIS

There are several diagnostic guidelines for polycystic ovary syndrome, and although different, each relies on combinations of 3 major elements to make the diagnosis: ovulatory dysfunction, hyperandrogenism (clinical or biochemical), and ovarian morphology. The National Institutes of Health (NIH)(41) and Androgen Excess Society (42) criteria emphasize the importance of androgen excess in the diagnosis, nothing that this identifies a phenotype at greater risk for metabolic complications. In contrast, the Rotterdam definition includes a phenotype that does NOT exhibit androgen excess: anovulation and polycystic ovarian morphology, but no hirsutism(43).

There are several nuances to consider in the diagnosis.

- Polycystic ovarian morphology, as defined by the Rotterdam criteria, requires transvaginal ultrasonography, which must demonstrate 12 or more follicles measuring 2-9 mm in diameter in each ovary, or increased ovarian volume (>10 mL) in the absence of a dominant follicle >10 mm.
- Testosterone measurements are often inaccurate in the normal female and polycystic ovary syndrome range, and the definition of “hyperandrogenemia” is often vague.

- While ovulatory dysfunction typically results in oligomenorrhea, many women with irregular ovulation have “regular” menses. Thus, a history of regular menses does not rule out polycystic ovary syndrome(42)

7.1 Cycle Control

Women with polycystic ovary syndrome have many of the established risk factors for endometrial cancer and its precursor, endometrial hyperplasia. These include irregular menses, lack of progesterone, unopposed estrogen exposure, obesity, insulin resistance, and diabetes. Women with polycystic ovary syndrome appear to have an almost threefold increased risk for endometrial cancer (44).

7.2 Polycystic Ovaries on Ultrasonography

Normal physiological changes and variations in the volume and size of the ovaries during puberty make ultrasonography findings controversial for the diagnosis of PCOS(45).

8. Treatment:

Lifestyle modification in polycystic ovary syndrome

It is well documented that modest weight loss (5–14%) via energy restriction improves CVD risk factors, hormonal profile and reproductive function in overweight and obese women with PCOS. Improvements include reductions in abdominal fat, blood glucose, blood lipids and IR(46-50), improvements in menstrual cyclicity, ovulation and fertility(46-53)

Exercise training

It is well known that exercise training improves an array of health-related outcomes, including protection against the development of CVD and diabetes, reduced morbidity and mortality(55-58), and psychological benefits including improvements in mood and psychological well-being(59-61).

Hormonal Therapy

If pregnancy is not desired, hormonal contraceptive agents containing estrogen and progestin can be used to provide endometrial protection and treat symptoms of hyperandrogenism. Cyclic therapy, such as oral contraceptives, induces regular withdrawal bleeding, thus preventing endometrial hyperplasia.

Anti-Androgen Therapy

Spironolactone (50-100 mg twice daily) effectively treats hirsutism. Spironolactone is often used in combination with oral contraceptives because of the additive effects of androgen suppression (oral contraceptives) and androgen blockade (spironolactone). Spironolactone is contraindicated during pregnancy because of potential teratogenicity

Metformin

Metformin has become a general treatment because it improves ovulation, insulin sensitivity, and possibly hyperandrogenemia(62). It is commonly used to treat infertility, either alone or in combination with clomiphene citrate. Because it increases ovulation in some women. The decision to prescribe this drug should be made on an individual basis (63).

CONCLUSION:

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age and can be associated with multiple long-term health risks and substantial psychological impact. Patients must be counseled regarding the long duration of treatment that includes lifestyle modifications along with systemic treatment. The risks of PCOS increases with the presence of one or more identified predisposing factors. Hence careful monitoring and proper management of identified predisposing factors not only delays but also helpful inadequate management of the disease.

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