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Review Article

Overview Of PCOS

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ABSTRACT

PCOS is a endocrine disorder which affect 6-15% female of the population globally. In PCOS condition ovaries develops more then ten cysts . It enhance the risk of infertility, cardiovascular diseases, gestational diabetes, hypertension, obesity, etc. its exact cause is unknown . It is prevented by some medication. Treatments are targeted toward improving the level of hyperandrogenism , insulin tolerance ,restoring menstrual cycle function, and improve fertility and major treatment should include weight management.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is one of the most common female endocrine disorders, affecting 6- 15% of the female population [1].It is mainly distinguished by a highly irregular menstrual cycle without ovulation. [2]. Hyper androgenic anovulation (HA) and Stein-Leventhal syndrome are other names for it. More than ten follicles can be seen on ultrasound in the ovaries of PCOS patients. The layer of the polycystic ovary has a thick center and more follicles than that of a normal ovary. This area, called the stroma, is where testosterone is produced. [1]. It was first described by Stein and Leventhal in 1935. PCOS etiology is complex, including genetic, environmental and lifestyle factors and remains controversial.Patients suffering from PCOS will consult for different degrees of hyperandrogenism (hirsutism, seborrhea, acne), dysfunction of the menstrual cycles, overweight, infertility.[3] It was thought that as people aged, PCOS changed from being a reproductive condition to being more metabolic, encompassing endometrial cancer (EC), metabolic syndrome (MS), diabetes mellitus (DM), hypertension (HT), visceral obesity, and dyslipidemia. [4][5] In clinical settings, 50% of women with PCOS experience recurrent pregnancy loss, and 75% of them have anovulation infertility. Endometrial cancer is more common in young women with PCOS-induced endometrial hyperplasia than in those without PCOS. PCOS's exact origin and pathophysiology are still

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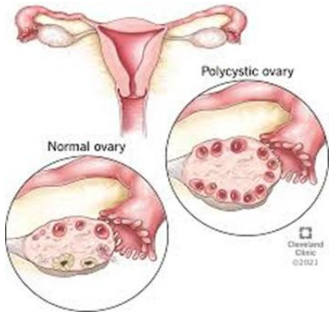
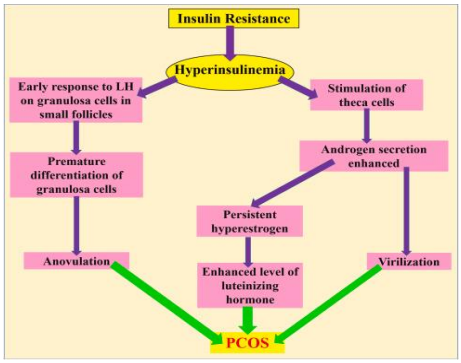
unknown. [6]. Ultrasound, magnetic resonance imaging (MRI), and computed tomography scanning (CT) are frequently used to detect PCOS. .[7] PCOS is a medical disorder where female sex hormones are out of balance. In other words, normal, high, or low amounts of estrogen along with higher levels of testosterone, DHEA-S, androstenedione, prolactin, and LH. Women with PCOS frequently have hyperinsulinemia, insulin resistance, and poor glucose tolerance; nevertheless, slim women with PCOS may also develop insulin resistance. [8].



Pathophysiology

The pathophysiology of PCOS is unknown, however the primary problem could be insulin resistance, resulting in hyperinsulinaemia. The main characteristic of the ovary is functional hyperandrogenism. Insulin and luteinizing hormone (LH) levels in the blood are typically elevated. This stimulation causes the theca cells, which surround the follicle and generate androgens that are then converted to oestrogen in the ovary, to become overly sensitive. They grow larger and manufacture more androgens than they need. The relatively high and constant oestrogen concentrations are assumed to be the origin of the rise in LH levels, which could change how the hypothalamic–pituitary axis regulates this hormone. The characteristic PCOS presentation of hirsutism, anovulation or dysfunctional bleeding, and malfunction of glucose metabolism can be explained by this combination of elevated levels of androgens, oestrogen, insulin, and LH. Ironically, the muscle and liver's insulin regulatory molecules are resistant to insulin, despite the theca cells' responsiveness..[1]



Clinical Manifestations

a) Hyperandrogenism-characterised by elevated levels of serum androgen.
b) Anovulation.
c) Metabolic disturbances.
d) 15% of females having irregular menstrual cycles.
e) Chronic anovulation
f) Hyperinsulinemia and decreased levels of SHBG
g) Infertility: due to chronic anovulation.
h) High levels of masculinizing hormones
i) Weight gain and obesity.
j) Male pattern baldness

k) High BP.
l) Pelvic pain

Risk factors :-

1. **Obesity**:- Studies have shown that between 30 and 70 percent of women with PCOS are obese. Additionally, studies show that PCOS women have higher levels of abdominal fat compared to weight-matched controls, which results in IR and hyperinsulinemia. To further control inflammation, adipose tissues release inflammatory mediators including cytokines. PCOS has been associated with elevated levels of TNF-α, interleukin-6, and CRP, all of which increase the risk of periodontal disease and cause persistent low-grade inflammation.[5]
2. **Endometrial cancer:-** Endometrial cancer is the most frequent gynecological cancer and the second most prevalent female malignancy in developed countries, however it affects only 4% of women under the age of 40. Histology is used to diagnose endometrial cancer. Although the underlying mechanism is yet unknown, females with PCOS have been found to have an elevated risk of endometrial cancer. Nevertheless, there is proof that the metabolic and endocrinologic abnormalities linked to PCOS may have intricate consequences on the endometrium, including an increase in the expression of steroid and androgen receptors that aid in endometrial dysfunction.Chronic anovulation in PCOS exposes the endometrium to prolonged unopposed oestrogen. Increased luteinizing hormone secretion, a defining feature of PCOS, may also be linked to the development of endometrial cancer, according to some research that found overexpression of of luteinizing hormone and human chorionic gonadotrophin receptors in uterine adenocarcinoma cells. [6].
3. **Cardiovascular disease :-** The metabolic syndrome is linked to polycystic ovarian syndrome (PCOS), which may raise the risk of cardiovascular disease (CVD) and its associated mortality in later life. There aren't enough studies on CVD and death in PCOS women who are long past menopause.[9]. A number of conventional risk factors for cardiovascular disease (CVD) are highly prevalent in women with PCOS. These include risk factors that can be controlled, like obesity, diabetes, hypertension, and dyslipidemia. CVD is not limited to men. In actuality, cardiovascular disease (CVD) kills one in three men and more women than the following five causes of mortality. Nine potentially modifiable risk factors were responsible for more than 94% of the population-attributable risk of a first myocardial infarction (MI) in women in the international INTERHEART research, which included patients from 52 countries. These included daily consumption of fruits and vegetables, regular alcohol consumption, regular physical exercise, psychosocial variables (such as depression, perceived stress, life events), smoking, dyslipidemia, hypertension, diabetes, and abdominal obesity. When taken as a whole, these results highlight the necessity of routine CV screening in PCOS-afflicted women in order to enable early interventions to reduce the overall cardio metabolic burden. [5]. According to certain research, women who exhibit suspected PCOS symptoms may be at higher risk for coronary artery disease (CAD).[9]
4. **Hypertension:-** Women with PCOS frequently have abnormal blood pressure regulation. A twofold increased risk of cardiovascular death is associated with prehypertension, which is defined as a

systolic blood pressure of 120 to 139 mm Hg or a diastolic blood pressure of 80 to 89 mm Hg. 24-hour ambulatory blood pressure measurements show that women with PCOS are more likely to develop prehypertension. Regardless of age, insulin resistance, obesity, or dyslipidemia, a Taiwanese investigation found that the hallmark hyperandrogenism of PCOS was linked to higher systolic and diastolic blood pressure. In general, high systolic blood pressure may occur independently of obesity and is identified after the third decade of life.[9]

5. **Dyslipidemia:-** The lipid profiles of women with PCOS are aberrant when compared to controls who are the same age and weight. The most prevalent lipid abnormalities are low levels of HDL-C and high triglycerides (TGs), which are both independent predictors of MI and CVD and closely associated with insulin resistance. Small, dense low-density lipoprotein cholesterol (LDL-C) particles that are atherogenic can also be identified by an elevated TG/HDL-C ratio. A TG/HDL-C ratio has been proposed as a straightforward metabolic diagnostic for identifying insulin-resistant overweight people. By showing a negative connection between TG/HDL-C and the quantitative insulin sensitivity index (QUICKI), we have validated this relationship in women with PCOS.6. According to our research, metabolic syndrome, a condition that predicts an elevated risk of cardiovascular disease and type 2 diabetes, can be identified with high sensitivity and specificity if TG/HDL-C > 3.2. It was recently demonstrated in a big trial (n > 1500) that TG/HDL > 3.5 can identify patients who are insulin-resistant and dyslipidemic and are therefore at a higher risk of CVD.[9]
6. **Gestational diabetes mellitus** - Gestational diabetes mellitus (GDM) and polycystic ovarian syndrome (PCOS) are the most frequent endocrine illnesses in women of reproductive age. Depending on the research populations and the diagnostic criteria used, the prevalence of PCOS ranges from 5% to 15% and that of GDM from 9% to 25%. Insulin resistance and being overweight or obese are linked to both conditions. Additionally, both illnesses are significantly influenced by hereditary factors.Both GDM and PCOS are linked to cardiovascular risk factors like metabolic syndrome, hypertension, and dyslipidemia, and they can serve as early indicators of an elevated risk of insulin-resistant diseases like type 2 diabetes (T2D). Although these illnesses share similar metabolic risks, it is yet unknown how PCOS functions independently and how common risk factors contribute to GDM. Regardless of the level of obesity, a number of studies have demonstrated that PCOS raises the risk for GDM. According to Mikola et al., being overweight was the best indicator of GDM, but PCOS also raised the risk of GDM on its own. Another study, however, found that women with PCOS who were not obese were not at risk for GDM. Additionally, two trials that included participants who were matched for age and BMI found no evidence of an elevated risk for GDM in PCOS-afflicted women. Despite these contradictory findings, the 2008 National Current Care Guidelines in Finland state that PCOS is a separate indication for an early oral glucose tolerance test (OGTT) during pregnancy, independent of BMI. The purpose of the current investigation was to elucidate the function of PCOS as a risk factor for GDM and to further test the validity of this strategy.[10]. Polycystic ovarian syndrome increases the

chance of incident postpartum diabetes in women with gestational diabetes. There was no correlation found between PCOS and incident diabetes in women without gestational diabetes. A history of both polycystic ovarian syndrome and gestational diabetes indicates an urgent need for diabetes surveillance and prevention, given the already heightened risk of diabetes in women with a history of gestational diabetes[11].

Treatments of PCOS:-

1. **Oral contraceptive (OC):-** For the long-term management of PCOS, these pills are the first line of treatment. Progesterone and estrogen make up the majority of these pills. In addition to suppressing ovulation by reducing LH, estrogen also raises the viscosity of cervical mucus, which stops sperm from penetrating and fertilizing the egg, and slows the development and maturation of ovarian follicles by inhibiting FSH and progesterone. Simultaneously, OCs have the ability to raise sex-hormonebinding globulin (SHBG) levels, which lowers free testosterone levels, lessens the peripheral function of androgens, and permits androgen deprivation. By improving hyperandrogenism and contraception, restoring the menstrual cycle, and protecting the endometrium, OC therapy can help prevent cancer.The following are now widely used clinical OCs: drospirenone/ethinylestradiol (Yasmin), cyproterone acetate/ethinylestradiol (Diane-35), and desogestrel/ethinylestradiol (Marvelon). According to some research, ethinylestradiol has more of an impact on liver metabolism than natural estradiol. This includes the production of angiotensin, SHBG, and certain estrogen-dependent blood coagulation factors. Scholars have started researching novel forms of estrogen, such as 17-estradiol, estradiol valerate, and estetrol, that resemble endogenous estrogen in form in order to counteract these metabolic consequences of OC therapy. More investigation and study are required for these initiatives. Long-term usage of OCs can raise the risk of venous thrombosis in PCOS patients who are not in need of reproduction. The risk of arterial thrombosis is low in patients who are not fat and have never smoked. Insulin-resistant PCOS patients are more likely to develop diabetes, but large-scale research indicates that the benefits of OC treatment outweigh the risks. According to a recent study by Harris et al., individuals with PCOS and irregular menstrual cycles are less likely to have an ovarian serous tumor; nevertheless, patients who have never received OC treatment or who are overweight are more likely to develop an ovarian serous border tumor..[12]
2. **Surgical Interventions :-**Sometimes, PCOS-related symptoms might be alleviated by surgical procedures. Patients who are extremely obese should be offered bariatric surgery since it is an excellent treatment for obesity and PCOS symptoms after all other choices have been exhausted. However, there are dangers, such as nutritional and surgical issues, and pregnancy should not be attempted within a year following the procedure. Laparoscopic ovarian drilling (LOD) is a minimally invasive laparoscopic surgery used to remove ovarian tissue using a surgical needle or a laser beam in order to improve and rebalance ovarian function in PCOS patients. Despite being uncommon, the operation is still an option for CC-resistant ovaries and situations where letrozole is not an option because of off-label use. But according to the current Cochrane Review, compared to medical ovulation induction alone, LOD may actually lower the live birth

rate in women with anovulatory PCOS and CC resistance, even while it lowers the risk for OHSS and the frequency of multiple pregnancies. It is also important to remember that LOD exposes women to surgical risks like adhesions, infection, and anesthesia-related problems. [13]

3. **Inositol treatment theory :-** Nestler et al. claim that traits in PCOS-afflicted women make their ovaries more active, which raises the conversion of myo-inositol (MI) to D-chiro-inositol (DCI) and lowers MI in the follicle. However, the study found that in MI, a fertilized egg had much more typical mature follicles or follicular fluid than immature or infertile follicles. Therefore, inositol therapy can improve the health of the ovarian follicles and menstrual cycles while also reducing insulin resistance in patients with PCOS. It is expected that this treatment would help future PCOS patients.[12].

Metformin,- When lifestyle changes are combined with PCOS, the majority of research suggests improvements in menstrual cycles, blood sugar levels, and obesity. Additionally, there is mild to moderate alleviation from insulin resistance and a modest to moderate improvement in lipid profiles. Metformin's low adverse event profile, affordability, and ease of use all promote its use. During patient visits, it is important to bring up gastrointestinal issues, the most common side effect of metformin, in order to ensure adherence to treatment. New research shows that obesity drugs, especially glucagon-like peptide-1 (GLP-1) receptor agonists, are more successful than metformin at treating obesity in women with PCOS, despite the fact that their high cost and accessibility limit their use. Future studies should concentrate on assessing the efficacy of combination therapies, such as GLP-1 receptor agonist and metformin, and forecasting the availability of these obesity drugs in low-income countries and regions.[14][15].

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