



OVERVIEW OF PCOS

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ABSTRACT

An endocrine condition known as PCOS affects 6–15% of women worldwide. More than ten cysts form on the ovaries in PCOS. It raises the risk of obesity, hypertension, gestational diabetes, cardiovascular disorders, and infertility, among other conditions. The cause of it is unknown. There are medications that prevent it. such as surgery, Inositol, oral contraceptives, and metformin.

Keywords: Polycystic Ovary Syndrome, Endometrial Cancer, Gestational Diabetes, Metformin, Obesity

The prevalence of PCOS, a complex endocrine disorder that affects 15–20% of women of reproductive age, varies depending on diagnostic and demographic factors [1]. Polycystic ovarian syndrome (PCOS) is frequently referred to as Stein–Leventhal syndrome since it was initially characterized by Stein and Leventhal in 1935[2].

To diagnose polycystic ovarian syndrome (PCOS), at least two of the three requirements must be met. These include polycystic ovaries on ultrasonography, hyperandrogenism, and oligo-ovulation or anovulation, which is defined as irregular or absent ovulation. The most widely used diagnostic standards are the Rotterdam criteria (2003) for This disease is associated with metabolic and hormonal problems, as well as an irregular ovulatory cycle, and often leads to infertility and other long-term health risks [3].

It describes a condition when at least one ovary produces an estimated ten small cysts with a diameter ranging from 2 to 9 mm and at least one ovary has an ovarian capacity of more than 10 millilitres [4].

According to estimates from the World Health Organization (WHO), PCOS affects about 116 million women worldwide (3.4%) [5]. Hypertrichosis, acne, and obesity associated with PCOS have a substantial impact on women's mental health. But irregular menstruation and amenorrhea can lead to reproductive dysfunction, which may eventually lead to infertility [6].

PCOS has been associated with several mental health conditions, including depression, anxiety, diminished sexual pleasure, and a deterioration in health-related quality of life (QoL) [7].

Hormonal imbalances include high insulin and testosterone levels, which have been linked to impulsivity, emotional reactivity, and appetite control, raise the likelihood of developing disordered eating practices. According to research, women with PCOS who struggle with body image are more likely to report higher anxiety levels, which has a detrimental effect on their general wellness, social relationships, and day-to-day functioning [8]. Research suggests that polycystic ovarian syndrome has a substantial genetic component that can be impacted by lifestyle choices, the gestational environment, or both, even if the precise cause of the condition is still unknown [9].

Obesity, type 2 diabetes, metabolic syndrome, hypertension, anomalies or macrosomia in the fetus (weight greater than 4 kg), thyroid, cardiovascular disease, dyslipidemia, and hyperplasia are long-term risk factors for PCOS. Endometrial cancer, psychological problems (such as anxiety or depression), pre-eclampsia, repeated

abortions, perinatal death, and potentially breast cancer are among the short- and long-term hazards. Clinical signs of this problem include hirsutism, irregular menstruation, uterine haemorrhage, alopecia, acne, and infertility. Variations in follicle-stimulating hormone (FSH), luteinizing hormone (LH), oestradiol, serum androgens (androstenedione and testosterone), high anti-Mullerian hormone (AMH), prolactin, and hyperprolactinemia further differentiate this syndrome. Furthermore, this disorder is associated with insulin resistance, a condition in which too much testosterone prevents the liver from producing sex hormone-binding globulin (SHBG), which lowers SHBG. On the other hand, low serum SHBG levels in PCOS patients are believed to be a biomarker of metabolic abnormalities and are linked to insulin resistance, hyperandrogenism, and inappropriate glucose metabolism. In addition to lengthening the menstrual cycle and increasing anovulation, hyperandrogenism also leads to amenorrhea, endometrial hyperproliferation, and maybe carcinogenesis. PCO, or the presence of at least 12 antral follicles (AFC) in the whole ovarian volume surpassing 10 mL, with a diameter ranging from 2 to 9 mm, is another important feature of PCOS women. Through a negative feedback loop of the gonadal axis, large amounts of oestrogen released by antral follicles may prevent the release of follicle-stimulating hormone (FSH), resulting in anovulation. Therefore, the length of the menstrual cycle and the number of antral follicles in the ovaries are the two main indicators to determine the severity of PCOS. The number of antral follicles and the duration of the menstrual cycle are closely correlated with the serum level of testosterone, suggesting that hyperandrogenism accelerates the onset and progression of PCOS(Figure 1) [10][11][12].



Figure 1: Polycystic ovary

Risk factors:-

Obesity: Research indicates that 30 to 70 percent of women with PCOS suffer from obesity. Furthermore, research indicates that women with PCOS have greater levels of abdominal fat than weight-matched controls, which leads to insulin resistance and hyperinsulinemia. Adipose tissues release inflammatory mediators, such as cytokines, to further regulate inflammation. Elevated levels of TNF- α , interleukin-6, and CRP have been linked to PCOS; these factors raise the risk of periodontal disease and result in chronic low-grade inflammation[13].



Figure 2: Obesity

Endometrial Cancer: Only 4% of women under 40 are affected by endometrial cancer, despite it being the most common gynaecological cancer and the second most common female cancer in affluent nations. Endometrial cancer is diagnosed through histology. Females with PCOS have been reported to have an increased risk of endometrial cancer, while the underlying mechanism is yet to be understood. However, there is evidence that the endocrinologic and metabolic abnormalities associated with PCOS may have complex effects on the endometrium, such as increased expression of androgen and steroid receptors that contribute to endometrial dysfunction. In PCOS, chronic anovulation exposes the endometrium to unopposed estrogen for an extended period of time. According to some research, uterine adenocarcinoma cells overexpress luteinizing hormone and human chorionic gonadotropin receptors, which may be associated to the development of endometrial cancer. Increased luteinizing hormone secretion is a characteristic of PCOS [14].

Cardiovascular illness: Polycystic ovarian syndrome (PCOS), which is related with the metabolic syndrome, may increase the risk of cardiovascular disease (CVD) and the mortality that goes along with it in later life. Studies on CVD and mortality in women with PCOS who are well past menopause are scarce [15]. Women with PCOS have a high prevalence of several traditional risk factors for cardiovascular disease (CVD). These include risk factors like obesity, diabetes, hypertension, and dyslipidaemia that are under control. Men are not the only ones with CVD. Actually, one in three men and more women die from cardiovascular disease (CVD) than from the next five causes of death. In the multinational INTERHEART study, which included patients from 52 countries, nine potentially modifiable risk variables accounted for over 94% of the population-attributable risk of a first MI in women. These included eating fruits and vegetables every day, drinking alcohol frequently, exercising frequently, smoking, having dyslipidaemia, high blood pressure, diabetes, and abdominal fat, as well as psychosocial factors like depression, perceived stress, and life events. All of these findings point to the need for regular cardiovascular monitoring in women with PCOS so that early interventions can lower the total burden of cardio-metabolic diseases. Some studies suggest that women with suspected PCOS symptoms may be more susceptible to coronary artery disease (CAD)[16].

Hypertension: Abnormal blood pressure regulation is common in women with PCOS. Prehypertension, defined as a systolic blood pressure of 120 to 139 mm Hg or a diastolic blood pressure of 80 to 89 mm Hg, is linked to a twofold increased risk of cardiovascular death. Prehypertension is more common in women with PCOS, according to 24-hour ambulatory blood pressure readings. According to a Taiwanese study, the characteristic hyperandrogenism of PCOS was associated with greater systolic and diastolic blood pressure regardless of age, insulin resistance, obesity, or dyslipidemia. Generally speaking, high systolic blood pressure is detected after the third decade of life and can happen without weight[17].

Dyslipidaemia: When compared to controls of the same age and weight, the lipid profiles of women with PCOS are abnormal. The most common lipid abnormalities are high triglycerides (TGs) and low HDL-C, which are strongly linked to insulin resistance and independent predictors of MI and CVD. Additionally, a high TG/HDL-C ratio can be used to identify atherogenic small, dense LDL-C particles. A simple metabolic diagnostic for determining whether an individual is overweight and insulin-resistant is the TG/HDL-C ratio. We have confirmed this link in women with PCOS by demonstrating a negative correlation between TG/HDL-C and the quantitative insulin sensitivity index (QUICKI).6. Our findings indicate that if $TG/HDL-C > 3.2$, metabolic syndrome, a condition that indicates an increased risk of cardiovascular disease and type 2 diabetes, can be detected with high sensitivity and specificity. A large experiment with over 1500 participants recently shown that $TG/HDL > 3.5$ can identify patients who are insulin-resistant and dyslipidemic, increasing their risk of cardiovascular disease[18].

Gestational diabetes mellitus:

The two most prevalent endocrine conditions in women of reproductive age are gestational diabetes mellitus (GDM) and polycystic ovarian syndrome (PCOS). Depending on the study populations and diagnostic standards used, the prevalence of PCOS and GDM ranges from 5% to 15% and 9% to 25%, respectively. Insulin resistance and being overweight or obese are linked to both conditions. In both illnesses, genetic factors are also important. Both GDM and PCOS are linked to cardiovascular risk factors like metabolic syndrome, hypertension, and

dyslipidemia and can serve as early indicators of an elevated risk of insulin-resistant conditions like type 2 diabetes. Even though the metabolic hazards of PCOS and GDM are similar, it is yet unknown how PCOS functions independently and how shared risk factors impact GDM. Regardless of the level of fat, PCOS raises the risk for GDM, according to numerous research. Being overweight was the best indicator of GDM, while PCOS alone raised the risk of GDM. However, a different study found that women with PCOS who were not overweight did not have an increased risk of developing GDM. Additionally, two trials that included participants who were matched for age and BMI showed no evidence of an elevated risk for GDM in women with PCOS. Despite these contradictory findings, PCOS is a clear indication for an early oral glucose tolerance test (OGTT) during pregnancy, regardless of BMI. The current study aimed to clarify the function of PCOS as a risk factor for GDM and evaluate the effectiveness of this strategy. Polycystic ovarian syndrome increases the chance of incident postpartum diabetes in women with gestational diabetes. There was no correlation between incident diabetes and PCOS in women without gestational diabetes. A history of both polycystic ovarian syndrome and gestational diabetes emphasizes the critical need for diabetes surveillance and prevention, given the already increased risk of diabetes in women with a history of gestational diabetes. [19][20].

MANAGEMENT OF PCOS

Oral contraceptive (OC):-

These pills are the first line of treatment for PCOS in the long run. Most of these medications contain progesterone and estrogen. Estrogen inhibits FSH and progesterone, which slows the development and maturity of ovarian follicles, increases the viscosity of cervical mucus, which prevents sperm from accessing and fertilizing the egg, and suppresses ovulation by decreasing LH. At the same time, OCs can increase levels of sex-hormonebinding globulin (SHBG), which reduces free testosterone, diminishes androgen peripheral function, and allows androgen deprivation. OC treatment can help prevent cancer by resuming the menstrual cycle, preserving the endometrium, and enhancing hyperandrogenism and contraception. Nowadays, drospirenone/ethinylestradiol (Yasmin), cyproterone acetate/ethinylestradiol (Diane-35), and desogestrel/ethinylestradiol (Marvelon) are the most often used clinical OCs. Some studies suggest that ethinylestradiol affects liver metabolism more than natural estradiol. This includes the synthesis of angiotensin, SHBG, and several blood coagulation components that are dependent on estrogen. To combat these metabolic effects of OC therapy, researchers have been studying novel forms of estrogen that mimic endogenous estrogen in form, such as 17-estradiol, estradiol valerate, and estetrol. These initiatives need further research and analysis. In PCOS individuals who do not require reproduction, long-term OC use can increase the risk of venous thrombosis. Patients who are not overweight and have never smoked have a low risk of arterial thrombosis. Diabetes is more common in those with insulin-resistant PCOS, although extensive evidence shows that the advantages of OC treatment exceed the dangers. An ovarian serous border tumor is more likely to develop in patients who have never received OC treatment or who are overweight, although those with PCOS and irregular menstrual cycles are less likely to have one, per a recent study[21].

Surgical Treatments:-

Surgical techniques may occasionally improve symptoms associated with PCOS. Since bariatric surgery is a great way to treat obesity and PCOS symptoms, it should be made available to patients who are exceedingly obese after all other options have been tried. However, pregnancy should not be attempted within a year after the treatment due to the risks, which include nutritional and surgical complications. To enhance and restore ovarian function in PCOS patients, laparoscopic ovarian drilling (LOD) is a minimally invasive laparoscopic procedure that involves removing ovarian tissue with a surgical needle or a laser beam. Although rare, the procedure is still a possibility for ovaries that are resistant to CC and in cases where letrozole is not a choice due to off-label use. However, despite lowering the risk for OHSS and the frequency of multiple pregnancies, the current Cochrane Review suggests that LOD may potentially reduce the live birth rate in women with anovulatory PCOS with CC resistance when compared to medical ovulation induction alone. It's also critical to keep in mind that LOD puts women at risk for surgical complications such as adhesions, infections, and issues associated with anaesthesia[22].

Exercise and physical activity:

It is yet another crucial element in PCOS management. Any skeletal muscle movement that requires the use of energy is considered physical exercise. Regular exercise, especially resistance and aerobic training, can help women with PCOS reduce body fat, enhance insulin sensitivity, and improve cardiovascular health. Exercise also has psychological benefits for those with PCOS. Moreover, several other methods, including acupuncture, naturopathy, and yoga (asana, breathing, mudras, and meditation), help women with PCOS manage their regular hormone levels and monthly cycles and reduce stress and anxiety[23].



Figure 3: Physical Exercise

Metformin: Most studies indicate improvements in menstrual periods, blood sugar levels, and obesity when PCOS is paired with lifestyle modifications. Furthermore, there is a slight to moderate improvement in lipid profiles and a mild to moderate reduction of insulin resistance. Metformin's use is encouraged by its minimal adverse event profile, cost, and simplicity of use. To guarantee adherence to therapy, it is crucial to discuss gastrointestinal problems, the most frequent side effect of metformin, with patients during visits. Despite their high cost and limited availability, new research indicates that obesity medications, particularly glucagon-like peptide-1 (GLP-1) receptor agonists, are more effective than metformin at treating obesity in women with PCOS. Future research should focus on predicting the availability of these obesity medications in low-income nations and areas, as well as evaluating the effectiveness of combo medicines like GLP-1 receptor agonist and metformin[24].

Inositol:

Inositol is a dietary supplement that aids with insulin management. How it regulates the biochemical and metabolic components of PCOS is unknown. Ovulation and menstrual periods can be improved, according to a recent study. Even though this advice advises against using it because of its limited benefits, inositol is cheap and has a low risk of side effects[25].

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