ISSN: 2755-0117

Journal of Oncology Research Review & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

An Overview of Harmful Effects of Polycystic Ovary Syndrome

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ABSTRACT

PCOS, a hormone imbalance that causes infertility, obesity etc. Polycystic ovarian syndrome (PCOS) is the most frequent endocrinopathy among women of reproductive age. It is the most common female endocrine disorder with prevalence rates ranging from 4% to 18%. There are many associated condition with PCOS like obesity, many types of cancer, infertility, cardiac diseases etc. It is confirm that women who have this syndrome are at risk more than other women. The treatment of PCOS is determined by whether a woman wishes to become pregnant or not. If pregnancy is not a goal, then weight loss, oral contraceptives, and the diabetes medication. It should also include all metabolic effects and potential problems. More study and knowledge of the biology of PCOS will lead to better treatment outcomes and patient management.

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Received: December 01, 2021; **Accepted:** December 09, 2021; **Published:** December 30, 2021

Keywords: Infertility, PCOS, Obesity, Cancer, Pregnancy

Introduction

PCOS, a hormone imbalance that causes infertility, obesity, and abundant facial hair in women, can also cause serious mental health problems such as anxiety, sadness, and eating disorders. Polycystic ovarian syndrome (PCOS), a group of symptoms that affects women of childbearing age, has reached epidemic proportions. This disorder caused by an imbalance in female sex hormones, causes cysts to form in the ovarian antral follicles. A cyst is a water-filled sac that contains the egg and should have been released for fertilization. Ovulation is prevented by the conversion of the egg into a cyst, known as a "functional cyst". When ovulation is inhibited, the menstrual cycle is disrupted, resulting in "amenorrhea". When numerous cysts develop in the ovarian follicles as a result of hormonal imbalance, this is known as PCOS. The size of the ovary grows because to water-retained cysts, some of which can be as large as 10mm broad. The absence of ovulation and the menstrual cycle hinders fertilization and conception, making pregnancy difficult [1, 2]. Even if implantation happens, the chance of abortion and stillbirth rises. Eclampsia and small-for-gestational-age infants are possible complications. PCOS can lead to pregnancy problems including gestational diabetes and pregnancy-induced hypertension [3].

PCOS is one of the most prevalent endocrine diseases in premenopausal women, affecting 5% of this group [4,5]. A unified definition of PCOS does not exist, owing to its varied and heterogeneous form. However, it is apparent to us that the problem is an endocrinopathy and that it should be referred to as PCOS, a syndrome rather than a disease 2 [6]. PCOS is an ovarian dysfunction or menstrual dysfunction condition. A recent study found that DENND1A, a potential gene for PCOS, was overexpressed in theca cells from PCOS patients [7]. Its defining characteristics are hyperandrogenism (i.e. presence of excess male hormone) and polycystic ovary (PCO) forms and chronic anovulation with the exclusion of particular adrenal, ovarian, or pituitary disorders [4,8,9]. Having the problem can have a major influence on women's quality of life during their reproductive years (5 - 20% women), and it adds to morbidity and death by the time they reach menopause. Menstrual abnormalities, indications of androgen excess, insulin resistance, compensatory hyperinsulinemia and obesity are some of the clinical findings. PCOS is linked to a higher risk of type 2 diabetes mellitus at an early age, insulin action anomalies (both insulin resistance and β-cell dysfunction) as well as later menopause and high prevalence of hypertension (40 %) [6,10,11]. Several lines of evidence show that women with PCOS are also more likely to develop cardiovascular disease [12]. There is now conclusive evidence that women with PCOS have a 37-fold higher chance of acquiring type 2 diabetes [11,13,14]. Endometrial cancer is considered to be more common in women with PCOS due to prolonged anovulation with unopposed estrogen exposure of the endometrium. However, there is a lack of epidemiological evidence to support this concept [15]. Women with PCOS are more likely to develop metabolic abnormalities and T2DM, as well as infertility, obstetrical difficulties, endometrial cancer, and mental problems. These women are also more likely to suffer cardiovascular and cerebrovascular problems, venous thromboembolism, endometrial cancer and ovarian cancer [16]. Clinical signs and symptoms of hyperandrogenism include hirsutism, acne, and androgenic alopecia. Obesity's influence on PCOS and PCOS's effect on

obesity are complicated, and substantial evidence of a relationship is currently absent. Despite the fact that PCOS may occur in both obese and lean women, a recent systematic review and meta-analysis showed that obesity was more common in women with PCOS than in women without PCOS [17]. Patients with PCOS are more likely to have problems during pregnancy. Depression and anxiety are more prevalent and severe in women having PCOS disorder than in non-PCOS women [18-20]. Women with PCOS exhibit dyslipidaemia as well as indicators of impaired vascular function [21-24].

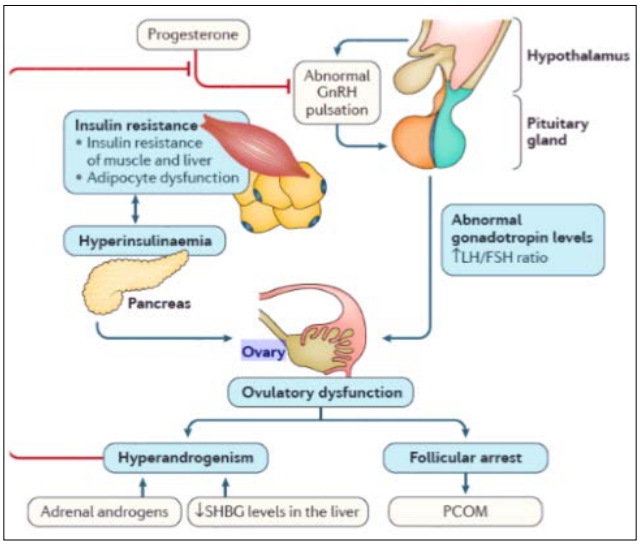

Figure 1: The pathophysiology of PCOS

The pulsatile release of gonadotropin-releasing hormone (GnRH) from the hypothalamus is frequently disrupted in polycystic ovary syndrome (PCOS), resulting in pituitary gland hypersecretion of LH, which causes ovulary dysfunction and hyperandrogenism. This erratic LH production appears to occur early in puberty and is linked to erratic suppression of GnRH secretion by progesterone. Although serum follicle-stimulating hormone (FSH) levels are typically normal, follicles in women with PCOS appear to be more resistant to FSH than in controls. This impact might be attributed to increased intra-ovarian anti-Müllerian hormone levels (AMH). Notably, genetic and epigenetic variations have a significant role in susceptibility to the majority of these changes. Environmental variables play a smaller role, mostly by increasing insulin resistance and disrupting gonadotropin secretion. PCOM stands for polycystic ovarian morphology, while SHBG stands for sex hormone-binding globulin [16].

Diseases and Conditions Associated with PCOS

Obesity affects around 60% of women with PCOS is well known. The central distribution of fat, on the other hand, is unaffected by BMI and is linked to greater insulin levels. The presence of a deficiency in insulin action that enhances LH-stimulated androgen release from thecal cells has been clearly established, independent of fat [25]. Insulin resistance appears to be the major underlying aberration that leads to the subsequent development of poor glucose tolerance. After the age of 30, it is estimated that more than 20% of obese women with PCOS would have impaired glucose tolerance [26].

The prevalence of type 2 diabetes is seven times higher in women with PCOS than in women without the condition. PCOS is hypothesized to have a higher prevalence of type 2 diabetes due to insulin resistance mixed with abdominal obesity. Non-obese women with PCOS, on the other hand, face a higher risk of acquiring type-2 diabetes [27]. As a result, PCOS is a risk factor for type 2 diabetes in middle age. PCOS is identified in the majority of women under 45 who have type-II diabetes. As a result, it's not unexpected that these women have a higher risk of gestational diabetes. Women with PCOS are thought to be at a higher risk that are also obese and require ovulation inducement to conceive. After pregnancy, women with gestational diabetes have been reported to have a significant frequency of PCOS [28].

Hyperinsulinemia appears to be the primary cause of PCOS women's elevated cardiovascular risk. In the absence of decreased glucose tolerance, there is pancreatic b-cell dysfunction that is inversely related to SHBG (sex hormone binding globulin) concentration, resulting in hyperandrogenism and prolonged unopposed estrogen secretion. The direct atherogenic impact is one route, whereas the unfavorable effect on the lipoprotein profile is another. Angiography shows that women with PCOS have more extensive coronary artery disease. PCOS-related hyperglycemia and impaired glucose tolerance are known risk factors for cardiovascular disease [29]. PCOS-related hyperglycemia and impaired glucose tolerance are known risk factors for cardiovascular disease. Women with polycystic ovaries have a highly skewed lipoprotein profile. They frequently have high triglyceride and total and low-density lipoprotein cholesterol levels in their blood [30]. On the other side, high density lipoprotein (HDL) levels, particularly HDL2 sub-fraction levels, are reduced. The amounts of serum plasminogen activator inhibitor-I are also elevated. The latter could inhibit fibrinolysis, affecting vascular tissue directly and generating alterations linked with coronary heart disease. The evidence is increasing that women with PCOS are at an elevated risk of developing cardiovascular disease. In the case of hypertension, there appears to be a link between insulin plasma levels and blood pressure. In women with PCOS between the ages of 40 and 59, the prevalence of treated hypertension is three times higher than in controls. Preeclampsia is four times more common in obese women with PCOS who become pregnant than in the general pregnant population20. Significant risk factors for atherosclerotic diseases, such as hypertension and myocardial infarction, appear to be present at a younger age in women with PCOS [31].

There has been a lot of discussion and concern regarding the risk of ovarian cancer in women who don't ovulate, especially because of the widespread use of medicines to induce ovulation in these people. There are several lines of evidence that point to a link between PCOS and an increased risk of ovarian cancer. Early menarche and late menopause tend to enhance the risk in nulliparous women. It's possible that stimulating repeated ovulations in women with infertility will raise their risk, but there's no evidence to back this up [32]. Although women with PCOS are thought to be in low risk categories for getting ovarian cancer due to their low ovulation rate over time, employing ovulation induction medications and producing multifollicular ovulations theoretically creates a risk imbalance for ovarian cancer [33]. According to another study associating clomiphene and ovarian cancer, women with PCOS have a relative risk of ovarian cancer of 4.1 when compared to controls. However, according to a big UK study, the standardized death rate for ovarian cancer is only 0.39 percent (95 percent CI 0.01-2.17) [34]. Even current evidence on the link between polycystic ovarian syndrome and ovarian cancer is contradictory, but generally reassuring [35].

The possibility of endometrial cancer being linked to PCOS has sparked renewed interest in the long-term hazards. The key reason for continued unopposed estrogen secretion and, as a result, a higher risk of endometrial cancer is thought to be prolonged anovulation, which characterizes the syndrome [36]. Obesity, long-term use of unopposed estrogen and progesterone, nulliparity, infertility, hypertension, and diabetes are all known risk factors for endometrial cancer. The majority of these factors have been linked to PCOS [37]. Adenocarcinoma may be preceded by endometrial hyperplasia. Although a precise estimate of progression rate is nearly impossible to calculate, it is predicted that 18% of adenomatous hyperplasia cases will progress to cancer in the next 2 to 10 years. Intervals of more than three months between menstruations in women with PCOS may be linked to endometrial hyperplasia and ultimate cancer [36]. The extra risk of endometrial cancer was shown to be 3.1 times higher in a large research involving 1270 women with chronic anovulation (95 percent CI, 1.1-7.3). However, a recent review of the data supporting a link between PCOS and endometrial cancer found it to be inconclusive [38]. The ultimate risk of endometrial cancer in PCOS-affected women is still unidentified [39]. Obesity, hyperandrogenism, and infertility are all known to be linked to breast cancer development. However, studies have found no evidence of a significant increased risk of breast cancer in women who have PCOS [40]. On the other hand, there appears to be a link between PCOS and a family history of breast cancer. The proportion of women having a positive family history of breast cancer was considerably greater in women with PCOS compared to controls in a sample of 217 women [41].

PCOS has key morphological features: an increase in the number of antral follicles and an increase in the size and density of the ovarian stroma. While some women with these ovarian traits are ovulatory, follicular growth stops once it reaches 5 to 8 mm in diameter for the majority of them. Anovulation and infertility are caused by the failure to produce a dominant follicle. The theca cells make up the majority of the dense ovarian stroma. The theca cells convert cholesterol to androgens via a series of intermediary steps, with the primary output being androstenedione followed by Progesterone, 17alpha-hydroxyprogesterone, and dehydroepiandrosterone. One of the primary causes of the hyperandrogenic ovarian milieu in PCOS patients is androgen overproduction by the theca cells in the ovaries, as well as hyperresponse to LH provocation by these cells. While androgen play an important role in follicle formation, hyperandrogenism has a negative impact on follicle growth leading to negative effects on ovarian function. Infertility is also caused by ovarian dysregulation. Vitamin D has long been linked to bone health and calcium and phosphorus balance, but evidence of vitamin D receptor expression in the ovaries, uterus, and placenta have suggested that vitamin D may also play a role in reproduction. The vitamin D receptor is found in granulosa cells, cumulus oophorus cells, endometrium, fallopian epithelial cells, placenta, and in the pituitary gland. The vitamin D pathway has been hypothesized to play a function in the regulation of PCOS symptoms. Calcitriol has been linked to follicular development and growth. It has also been shown to increase insulin receptor expression, insulin synthesis and secretion, and insulin sensitivity. Although the presence of vitamin D receptor polymorphisms has been linked to the severity of PCOS phenotype; these findings are controversial and need further investigation.

Mitochondria are the cell's functional "power House" and play a fundamental role in cell energy metabolism, apoptosis, and signal transduction for cell proliferation. Follicular fluid is complex fluid that contains a mixture of protein, sugar, reactive oxygen species, antioxidants, and hormones. Oocytes contains a large number of mitochondria which play an important regulatory role in oocyte maturation, fertilisation, and embryo development before implantation. Oocyte maturity and quality are directly affected by the concentration of these substances. Imbalances in antioxidant factors and reactive oxygen species in the follicular fluid can have adverse effects on Oocyte quality, fertilization, and embryo development. This process, which results in abnormal ovulation and infertility in PCOS patients, is most likely caused by the disruption in the follicular microenvironment's equilibrium. Numerous oxidative stress indicators are abnormal in the blood and follicular fluid of patients with PCOS and may play a role in infertility among these women.

Menstrual periods usually lasts four to seven days. Examples of menstrual problems include periods that occur less than 21 days or more than 35 days apart, missing three or more periods in row (Amenorrhea), and menstrual flow that is much heavier or lighter than usual (Menorrhagia).

In polycystic ovary syndrome (PCOS), the ovaries make large amounts of androgens (male hormone). Small fluid-filled sacs (cysts) may form in the ovaries. These are oftenly seen on an ultrasound. Because the hormonal changes can prevent eggs from maturing, ovulation may not occur consistently. A woman with polycystic ovary syndrome may experience irregular periods or stop menstruating completely. Furthermore the condition is linked to obesity, infertility and hirsutism (excessive hair growth and acne). Although the exact cause is unknown, This condition may be caused by a hormonal imbalance.

Long-term Health risks of PCOS

It has been observed that women with PCOS have to face many long-term health problems than other women whose menstrual cycles are normal. The risk of hyperinsulinaemia (metabolic defect) and cardiovascular diseases are more incident. Up to 80% of women with PCOS are those with insulin resistance. The elevated production of insulin which is supposed to maintain normal blood glucose levels, cause the excessive production of androgens which leads to a condition known as hyperandrogenism, a characteristic of polycystic ovarian syndrome. High production of androgens can cause arrest of premature follicular growth. The elevated levels of insulin promote fats accumulation in adipose tissue and hinder to release these fats, as a result of which chances of obesity are increased which further promotes insulin resistance. Various medications have been designed to increase insulin sensitivity e.g. metformin, which are being proven effective against metabolic and hormonal imbalances and preferred in treatment of the syndrome [42].

The risk of cardiovascular diseases is supposed to be found greater in women with PCOS with impaired cardiac structure and function, cardiopulmonary impairment, lipid irregularities and other cardiac abnormalities. A critical and careful investigation is required to cope with these long term abnormalities [43] .

Women suffering from PCOS even with no obesity and normal body weight, have heart size considerably larger than the normal women. PCOS women have lower left ventricular ejection fraction (LVEF) which is considered as a measure of systolic function, and reduced early atrial mitral flow velocity as a measure of diastolic function, although all patients have normal LVEF overall. These patients have higher levels of diastolic blood pressure (DBP) as compared to healthy women. This suggests that the protracted high blood pressure could increase left ventricular size [44].

It is well known that reduced functional capacity is associated with an increased risk of cardiovascular mortality. The maximal oxygen consumption (VO2max), is closely and directly related to insulin sensitivity and a strong determinant of the insulin sensitivity index. Testosterone levels also positively correlate with (VO2max) although little is known about how testosterone might have an effect itself or influence insulin action. However, it is well recognized that exercise improves glucose homeostasis related to an up-regulation of the expression and/or activity of proteins involved in insulin signal transduction in skeletal muscle. To date, only two experimental studies have demonstrated a significant reduction in (VO2max) in young women with PCOS, when compared with healthy women, showing an impaired cardiopulmonary pattern leading to reduced cardiopulmonary functional capacity in these patients [45].

Treatment

The treatment of PCOS is determined by whether a woman wishes to become pregnant or not. If pregnancy is not a goal, then weight loss, oral contraceptives, and the diabetes medication Metformin® (an insulin sensitizer) can regulate a woman's cycles. Ovulation-stimulating medications can be tried if pregnancy is desired.

PCOS is strongly linked to infertility one of the most common reasons for women seeking medical attention. For women with PCOS related infertility, treatment options include oral ovulation-induction agents, controlled ovarian stimulation, and IVF. The goal of ovulation induction is to recruit a single follicle in order to reduce the risk of multiple gestations. Because of the high risk of multifollicular recruitment, the possibility of multiple gestations and ovarian hyperstimulation syndrome, PCOS patients undergoing fertility treatment should be closely monitored. When a patient's reaction is thought to be too high, cycle cancellation should be discussed with them. If ovulation-induction treatments fail, IVF is an option. Although ovarian hyperstimulation is of concern given the high number of follicles reported in PCOS women, IVF methods that take into account gonadotropin dose and the use of GnRH agonists triggers have significantly decreased the risk of ovarian hyperstimulation syndrome. Furthermore, IVF allows for a single embryo transfer lowering the risk of a twin pregnancy significantly. As a result, for women with PCOS, stepwise treatment plan should be developed with a strong focus on treatment modality based on risk/benefit stratification.

Conclusion

The current diagnostic recommendations are still ambiguous, and patients with less severe non-classic characteristics may go undetected. Adolescent standards are insufficiently specific, and they may fail to distinguish between normal development and disease. Because accurate diagnosis is essential for initiating therapy and preventing future morbidity, more clinical research should be conducted to not only update and unify guidelines, but also to offer a justification for diagnostic technologies that can detect all PCOS phenotypes.

Finally, we believe that this analysis offers an updated summary that clarifies the complex nature of PCOS. Future research should concentrate on filling in the gaps in our developing understanding of this disorder so that physicians can provide the best possible care to patients. PCOS requires proper diagnosis and management because it carries a number of metabolic and cardiovascular concerns if not treated properly. The underlying pathophysiology of PCOS is clearly not well understood. As a result, treatment is frequently centered on individual symptoms rather than the illness as a whole. However, as the pathophysiology of PCOS is better understood, so is the treatment should be tailored to the individual, it should also include all metabolic effects and potential problems. More study and knowledge of the biology of PCOS will lead to better treatment outcomes and patient management.

Funding

No.

Conflicts of interest

There are no conflicts of interest.

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