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Review

Polycystic Ovary Syndrome (PCOS): A Breif Review On Their Etiology, Complications and Treatments

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Abstract

Stein and Leventhal published the first description of polycystic ovarian syndrome (PCOS) in 1935. This condition is often referred to as Stein-Leventhal syndrome. Four to twenty percent of women around the world are affected by this condition, which is one of the most prevalent endocrine and metabolic illnesses that has an impact on the reproductive health of women. In addition to insulin resistance, obesity, infertility, and an increased risk of metabolic, endometrial, and cardiovascular consequences, polycystic ovary syndrome (PCOS) is characterised by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology. PCOS presents with a broad clinical spectrum. There are still other factors that contribute to the development of polycystic ovary syndrome (PCOS), including genetics, lifestyle choices, and environmental influences. Insulin resistance and hyperinsulinemia are two of the most important contributors to the pathophysiology of PCOS. When making a diagnosis, the Rotterdam criteria are the primary considerations. A multidisciplinary approach is emphasised in the current management strategies. This approach combines lifestyle modifications (such as weight loss and exercise), pharmacotherapy (such as metformin, oral contraceptives, inositol, selenium, letrozole, and clomiphene citrate), and assisted reproductive technologies for infertility, such as bariatric surgery and laparoscopic ovarian drilling.

Keywords: PCOS, Cardiovascular disease, Gestational diabetes, Oral contraceptive pills, Endometrial cancer

INTRODUCTION

The disorder was first defined extensively through Stein and Leventhal in the year 1935 [1]. Polycystic ovarian syndrome (PCOS), which is often referred to as Stein-Leventhal syndrome [2], is one of the metabolic and endocrine diseases that has the greatest impact on the reproductive health of women. Around the world, it affects between 4% and 20% of females. The characteristics that are most commonly associated with polycystic ovarian syndrome are polycystic ovaries, hyperandrogenism, and irregular menstruation, as stated by the Rotterdam criteria, which are largely accepted. Four. The symptoms of polycystic ovarian syndrome (PCOS), which include hypertrichosis, acne, and obesity, have a significant impact on the mental health of women. Amenorrhoea and irregular menstruation can both lead to reproductive issues, including infertility, which can occur simultaneously[5].

Polycystic ovarian syndrome (PCOS) has been linked to a number of psychological difficulties, including diminished sexual pleasure, anxiety, sorrow, and overall health-related quality of life (QoL) [6]. There is research that supports this connection.

Since polycystic ovary syndrome (PCOS) increases the risk of various comorbidities, such as obesity, insulin resistance, diabetes, and cardiovascular disease, it has the potential to exacerbate the health and economic implications that are experienced on a global scale [7].

The majority of women who have polycystic ovarian syndrome (PCOS) experience irregular menstrual periods. However, even individuals who have regular cycles can still experience oligo-ovulation, and ovulatory dysfunction that is characteristic of PCOS is a hallmark of the condition [8]. Hormonal abnormalities, such as raised insulin and testosterone levels, as well as characteristics such as impulsivity, emotional reactivity, and the regulation of appetite, have been linked to an increased risk of developing disordered eating practices. According to research, women who have polycystic ovarian syndrome (PCOS) and have low self-esteem are more likely to suffer anxiety. This, in turn, has an effect on their capacity to function on a daily basis, their relationships with other people, as well as their general health and happiness [9]. There is a considerable inherited component that is regulated by environmental factors during pregnancy or lifestyle choices, or both; nonetheless, the precise genesis of polycystic ovarian syndrome is still a mystery [10]. Research indicates that this component is influenced by environmental factors. Insulin resistance can range from minor to severe in persons who have polycystic ovarian syndrome (PCOS). Insulin resistance affects approximately 27% of women in the general population; however, this percentage can increase to between 50 and 80 percent in women who diagnose themselves with polycystic ovarian syndrome. The prevalence of insulin resistance ranges from approximately 70–95% among obese PCOS women and from 30–75% among PCOS women who have normal weights. Elevated insulin levels are not only a sign of polycystic ovarian syndrome (PCOS), but they are also the primary cause of the condition [11].[12].

The production of hepatic sex hormone binding globulin (SHBG) is decreased by hyperinsulinemia, which in turn leads to an increase in the levels of free and bioactive androgens in the blood. Additionally, hyperinsulinemia amplifies the effect of luteinizing hormone (LH) on ovarian cells, which in turn leads to an increase in androgen synthesis, in addition to other concerns related to metabolism and cardiovascular health. [13] Research has shown that women who have hyperandrogenism experience a considerable acceleration in the advancement of metabolic disorders. It is [14]. Because of hyperandrogenism, the menstrual cycle is getting longer and longer. This leads to an increase in the frequency of anovulation, which in turn leads to amenorrhoea, endometrial hyperproliferation, and cancer. One further significant trait that is present in women who have polycystic ovarian syndrome (PCOS) is the presence of the condition. This is characterised by the presence of twelve or more antral follicles (AFC) with a diameter that falls between two and nine millimetres and an ovarian volume that is greater than ten millilitres. In cases where there are an excessive number of antral follicles, which then secrete an excessive amount of oestrogen, anovulation may take place. A negative feedback loop in the gonadal axis is responsible for the subsequent decrease in the release of follicle-stimulating hormone (FSH) that occurs as a result of this.

Both the length of time that a woman has been menstruating and the number of antral follicles that are present in her ovaries are primary indicators that can be used to evaluate perimenopausal symptoms. Figure 1 illustrates a positive correlation between blood testosterone level and menstrual cycle duration as well as antral follicle count. This correlation may suggest that hyperandrogenism plays a role in the onset and progression of polycystic ovarian syndrome on account of its association with these factors. [15] and [16].

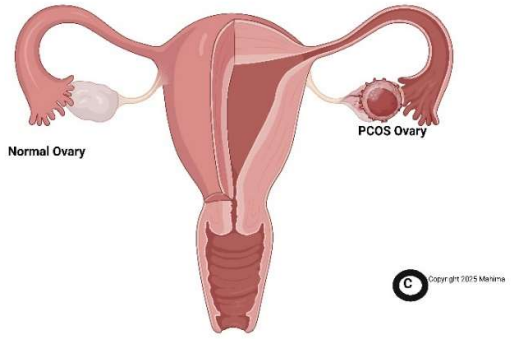

Fig 1: Normal & PCOS Ovaries of female reproductive parts created by Biorender

Etiology of pcos

Whenever it comes to the etiology of this illness, the elements that are involved are both hereditary and environmental. Risk of polycystic ovary syndrome (PCOS) is increased by an unhealthy lifestyle, food, or any viral mediators. The ovarian function is disrupted, and the levels of androgen rise, which ultimately results in anovulation [17]. This is because insulin resistance and its elevated level are the cause of the problem.

Gene factor

A total of 11 genetic loci that have been linked to polycystic ovary syndrome (PCOS), according to genome-wide association studies (GWAS) [18]. A total of roughly twenty common susceptibility variants for polycystic ovary syndrome (PCOS) were discovered using genome-wide association studies (GWASs) in Chinese and European populations [19]. Among the candidate genes are receptors for luteinizing hormone/choriogonadotropin (LHCGR), follicle stimulating hormone (FSHR), insulin (INSR), and beta subunit of follicle stimulating hormone (FSHB). Additionally, there are loci that are associated with the development of type 2 diabetes (THADA, HMGA2) and type 1 diabetes (RAB5B, SUOX, ERBB3). These loci are also involved in the development of ovarian follicles, androgen biosynthesis, and metabolic regulation. Among sisters of women who have polycystic ovary syndrome (PCOS), it has been demonstrated that metabolic variables, such as body mass index (BMI) and insulin resistance, indicate a significant degree of heritability. Additionally, the specific hormonal components of polycystic ovary syndrome (PCOS) are strongly heritable, including testosterone, dehydroepiandrosterone sulphate, and sex hormone-binding globulin [20]..

Enviromental conditions

There is a limited understanding of the role that geography plays in determining the prevalence or presentation of polycystic ovary syndrome (PCOS), such as the proximity to large bodies of water, altitude, latitude/longitude, climate, or terrain. Other factors that may be responsible for determining the prevalence or phenotype of PCOS include environmental toxins and socioeconomic status.

Hyperinsulinemia.

Insulin is the primary hormone that is responsible for both the process of lipogenesis and the maintenance of glucose homeostasis. The hormone insulin not only has an effect on the metabolism of carbs, lipids, and proteins, but it also has the ability to stimulate the production of new cells. Insulin receptors, which are found in a variety of tissues around the HPO axis, are responsible for mediating the actions of insulin. Insulin has the ability to enhance the activity of the trophic hormones that are present in steroidogenic tissues, such as the adrenal cortex and the ovary, which in turn stimulates the production of steroids [22]. Hyperinsulinemia is the primary cause of excessive androgen production. This is due to the fact that insulin directly mimics the effect of LH and indirectly elevates GnRH to a higher level. Insulin has the effect of lowering the levels of a crucial circulatory protein called sex hormone binding globulin (SHBG), which is responsible for regulating testosterone levels. Therefore, reduced levels of SHBG would result in increased amounts of free androgens, which are the factors that induce clinical signs of polycystic ovary syndrome (PCOS), such as acne, hirsutism, and alopecia [23]. Figure 2.) [25].

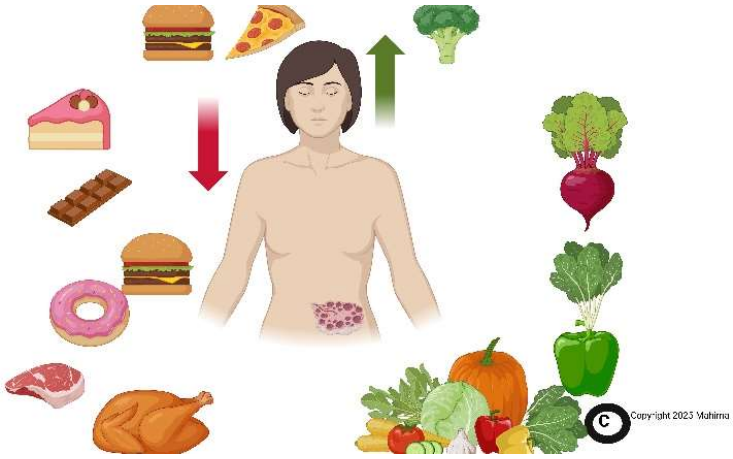

Fig 2: Diet plan for health lifestyle created by biorender

Epidemiological studies

Subsequently is essential to point out that the prevalence of polycystic ovarian syndrome, generally referred to as PCOS, varies from region to region around the globe. When compared to the global average, the prevalence of polycystic ovarian syndrome (PCOS) in India ranges from 2% to 35%, while it is anywhere from 4% to 21% worldwide. A number of factors, including population ethnicity, geographic location, diagnostic criteria, and variances in androgen and ultrasonography-based exams, contribute to the wide range of variability that can be observed in the prevalence of polycystic ovary syndrome (PCOS). To this day, however, there has not been a single population-based investigation that has included a sample size that is sufficiently big to draw any definitive conclusions regarding the prevalence of PCOS [26].

Indications for the Rotterdam Criteria include the most successful therapeutic therapy for polycystic ovarian syndrome (PCOS) and the method to obtain the most precise diagnosis of specific phenotypes of this condition. These are the current indications for the Rotterdam Criteria. The results of an investigation about the prevalence of polycystic ovarian syndrome in 204 countries from 1990 to 2019 were made public by researchers in the year 2022. Beginning in 1990, the point and yearly age-standardized PCOS incidence rates over the world have increased by nearly thirty percent, and this trend is expected to continue until 2019. As per the findings of the research conducted on the Global PCOS Treatment Market, Forecast & Opportunities, the number of individuals affected by polycystic ovarian syndrome (PCOS) will potentially reach roughly 5.1 million by the year 2025. There appears to be a connection between the rise in the prevalence of this syndrome and the following conditions: insulin-glucose metabolism abnormalities, obesity, oxidative stress as a result of selecting an unhealthy lifestyle and consuming an excessive amount of simple carbohydrates in the diet, and diabetes mellitus (DM) [27].

Through the use of the Rotterdam criterion, the inquiry came to the conclusion that the prevalence was 4.21 percent. In addition, the findings demonstrated that women who lived in urban districts had a higher incidence of polycystic ovarian syndrome in comparison to those who lived in rural areas. The increased prevalence of polycystic ovarian syndrome (PCOS) may be attributed, at least in part, to the sedentary lifestyle and poor eating habits that are typical of those who live in urban areas. Through the application of the Rotterdam criterion, a frequency of 6% was discovered. It would appear that the incidence of polycystic ovary syndrome was higher among women of Indian descent than it was among women of American descent.

Due to the fact that the vast majority of epidemiological research on the subject have been conducted in industrialised nations, there is a minimal amount of information available regarding the prevalence of polycystic ovarian syndrome (PCOS) in the Middle East and North Africa region. There has been a wide range of rates of polycystic ovarian syndrome (PCOS) observed in small samples in a few Western European countries [28]. These rates range from 2.3% to 28%. It was discovered by researchers in South India that 9.13% of students studying health science were affected by polycystic ovary syndrome. According to the survey, seven percent of Omani women who were diagnosed with polycystic ovary syndrome were between the ages of twelve and forty-five. Self-reported prevalence was determined to be 25.9% in the United Arab Emirates, according to recent research. Between the years 1990 and 2019, a study conducted in the Middle East and North Africa region found that the frequency has increased by 37.9 percent. The worrisome increase in the number of occurrences has led some people to hypothesise that the cause is a shift in lifestyle factors such as stress, dietary changes, and other lifestyle issues [29]. According to the diagnostic guidelines established by the National Institutes of Health, the prevalence of polycystic ovarian syndrome (PCOS) has increased from 6% to 9% in a number of nations, including the United States of America, the United Kingdom, Spain, Greece, Australia, Asia, and Mexico [30].

Clinical features/Signs and Symptoms of PCOS[31]

- Sleep problem
- Hair fall
- Fatigue
- Acne
- Infertility
- Hirsutism
- Obesity
- Anxiety
- Depression
- Hyperinsulinemia
- Hyperandrogenism
- Cancer
- Improper periods
- Gestational diabetes
- Polycystic ovaries[31]

Difference between pcod & pcos

Polycystic ovary syndrome (PCOS) is a metabolic syndrome, whereas polycystic ovary syndrome (PCOD) is a less severe sickness that can be cured with the right diet and exercise. In comparison to polycystic ovary syndrome (PCOS), polycystic ovary syndrome (PCOS) is associated with a higher risk of comorbidities, including insulin resistance, diabetes, cardiovascular issues, and endometrial cancer. Although polycystic ovary syndrome (PCOS) is characterised by a smaller number of symptoms, the symptoms of polycystic ovary syndrome (PCOS), which include acne, weight gain, and abundant facial hair, are noticeable at a younger age. Women who have polycystic ovary syndrome (PCOS) do not have many challenges when it comes to becoming pregnant because they have access to medical care, which can be of great assistance; but, they are more likely to encounter infertility and miscarriage. In spite of the fact that their symptoms are similar to those of PCOS, women who have PCOD may still ovulate. On the other hand, the acute hormonal imbalance that occurs in the latter circumstance works to prevent ovulation. Patients with polycystic ovary syndrome (PCOS) have ovaries that are big, thick, and have a high volume, and they have between 12 and 15 cysts. Ovaries that are affected by polycystic ovary syndrome (PCOS) may not be very big and may have anywhere from five to eight cysts. [32] [32]

Complications associated - with pcos

Endometrial cancer and endometrial hyperplasia

Amenorrhoea is a prevalent sign among women who have polycystic ovary syndrome (PCOS). If it is not treated effectively for an extended period of time, it can progress into endometrial hyperplasia and endometrial cancer. One of the conditions that affects the female reproductive system is called endometrial hyperplasia. The presence of an abnormally high number of cells, known as hyperplasia, causes the lining of the uterus to grow abnormally thick. But in women who have polycystic ovary syndrome (PCOS), it raises the risk of developing endometrial cancer shows in (Figure 3) [33].

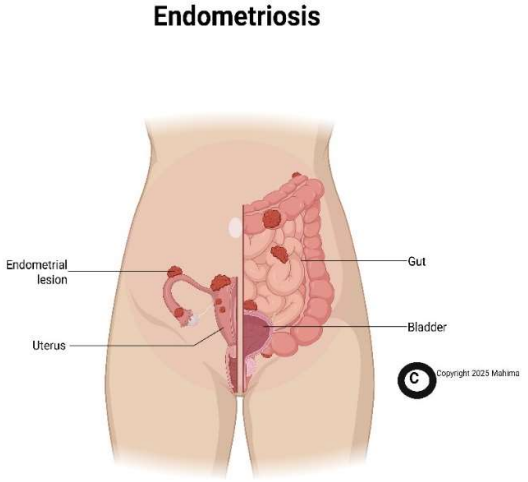

Fig 3: Shows that Endometrial cancer cause by delayed treatment of PCOS fig draw by Biorender

Cardiac- dysfunctions

Cardiovascular disease, also known as heart attack or stroke, is a significant worldwide health problem that impacts millions of individuals all over the world and places a significant financial burden on healthcare systems. Additionally, polycystic ovarian syndrome (PCOS) may boost the risk of cardiovascular disease [34]. The phenotypes of polycystic ovary syndrome (PCOS), insulin resistance, hyperinsulinemia, excessive exposure to androgens, and ovarian function are all factors that have been linked to an elevated risk of cardiovascular disease in women who have PCOS. Insulin resistance is linked to the inactivation of nitric oxide (NO) after it has been released from endothelial cells, as well as a decrease in the generation of nitric oxide (NO) and an increase in the synthesis of vasoconstricting substances in excessive levels. All of these abnormalities result in reduced vasodilatation and stiffness of the heart muscle. In addition, hyperinsulinemia and insulin resistance both exhibit hypertrophic effects directly and are associated with endothelial dysfunction. The community of people with PCOS was found to have an elevated risk of heart dysfunctions, according to clinical research [35].

Appiettite

Inherited, psychological in nature endocrinological, and metabolic variables are thought to be involved in the development of eating disorders in women who have polycystic ovary syndrome (PCOS). According to the findings of a previous study, women who have polycystic ovary syndrome (PCOS) had a three to six times higher risk of having eating disorders when compared to women who were in a control group. Both bulimia nervosa and binge eating disorder are significantly connected with polycystic ovary syndrome (PCOS), which is a condition that affects the digestive system. However, the method that is used to diagnose eating disorders differs from study to study, therefore it is not possible to simply compare the frequency of eating disorders across different racial and cultural groups. Further research is required to determine the extent to which phenotypic differences in PCOS, as well as racial and ethnic disparities, are associated with eating disorders [36].

Brain disorder (depression)

When compared to controls who did not have a body mass index that was the same, women with polycystic ovary syndrome (PCOS) were found to have a higher incidence of depressive symptoms. Women with polycystic ovary syndrome (PCOS) had much greater rates of major depression, recurring depression, and attempts at suicide. It is important to conduct screenings and diagnose those who suffer from anxiety and depression. Treatment that is appropriate ought to be administered [37].

Being diagnosed with obesity

Numerous studies have shown that between 33 and 88 percent of women who have polycystic ovary syndrome (PCOS) are either overweight or obese. This finding shows that there is a substantial connection between obesity and PCOS. It is believed that obesity can contribute to insulin resistance and raise your risk of having polycystic ovary syndrome (PCOS) [38], however the exact relationship between the two is not well understood but is thought to be related.

Type II diabetes mellitus during the course of pregnancy

In women who have polycystic ovary syndrome (PCOS), the most common pregnancy complication is gestational diabetes mellitus (GDM), which has a risk that is two to three times higher than the risk for women who do not have PCOS, regardless of their body mass index (BMI) [39]. Diabetes mellitus (GDM) is characterised as inadequate glucose tolerance that is initially identified during pregnancy [40]. Because of the rise in obesity, the prevalence of type 2 diabetes is on the rise. It is estimated that 14% of people throughout the world have the condition, with the percentage ranging from 1% to 28% depending on factors such as ethnicity, screening methods, and diagnostic criteria [41], [42]. There is a correlation between gestational diabetes mellitus and unfavourable pregnancy outcomes for both the mother and the infant. These outcomes include preeclampsia, premature birth, shoulder dystocia, macrosomia, big for gestational age (LGA) infant, and neonatal hypoglycemia [43], [44]. An higher risk of unfavourable pregnancy outcomes is associated with both polycystic ovary syndrome (PCOS) and gestational diabetes mellitus (GDM) in women; however, it is not well understood if the combination of these two disorders makes the dangers for mothers and infants even more severe. In light of this, the purpose of this study is to explore pregnancy and neonatal outcomes among women who have either PCOS-only, GDM-only, or the combination of PCOS and GDM, and to determine the risks associated with these conditions [45]

PCOS – management

Weight reduction: In those who are overweight or obese, a weight decrease of 5%–10% helps alleviate the severity of symptoms such as menstruation irregularities, acne, hirsutism, and alopecia. No explicit dietary or exercise guidelines for PCOS exist, and healthcare providers must be acutely aware of weight stigma, as individuals with PCOS are susceptible to distorted body image and disordered eating behaviours.

Physical activity and exercise are crucial for weight loss

They may enhance insulin sensitivity [47]. Numerous studies propose differing durations for weekly exercise; nevertheless, the American Heart Association (AHA) advocates for roughly 150 minutes of moderate or 75 minutes of vigorous activity each week. Numerous studies indicate that exercise, regardless of dietary intervention, can restore ovulation in women with PCOS. Exercise likely influences ovulation via modulating the hypothalamic-pituitary-gonadal (HPG) axis. In overweight and obese women, physical activity results in decreased insulin and free androgen levels, facilitating the reestablishment of hypothalamic-pituitary-adrenal control of ovulation [49].

Inositol

Inositol, a nutritional supplement, facilitates insulin signalling. The extent of its involvement in the regulation of the metabolic and biochemical aspects of PCOS remains inadequately understood. A recent study indicates that menstrual cycles and ovulation can be enhanced. This suggestion advises against the use of Inositol due to its modest benefits; yet, it presents a minimal risk of unwanted effects and is cost-effective.

Saraca Asoka

The primary application of Ashoka bark is in the management of PCOS, irregular menstruation problems, heavy bleeding, uterine spasms, mild to severe discomfort, and dysmenorrhea. Asoka is regarded as one of the premier uterine tonics, aiding in the regulation of irregular menstrual cycles and addressing instances of miscarriage. The plant is utilised to avert excessive bleeding or menorrhagia. Women with PCOS and various uterine disorders utilise both the flower and bark components.

Vitamin D

It has demonstrated therapeutic efficacy in the management of PCOS, contingent upon the prognosis of the condition. Vitamin D markedly augments insulin production and elevates insulin receptor expression while inhibiting pro-inflammatory cytokines, hence enhancing glucose metabolism [52]. The impact of Vitamin D on metabolic and reproductive dysfunctions in PCOS may be mediated via its overall effect on insulin resistance. In comparison to the placebo group, Vitamin D administration markedly decreased fasting plasma glucose, and there was a notable enhancement in insulin resistance and serum fasting insulin levels. Furthermore, four studies revealed a significant reduction in the mean blood triglyceride level [53].

Infertile women with PCOS eligible for IVF received 50,000 IU of Vitamin D biweekly for 8 weeks, leading to significant decreases in serum levels of AMH and insulin. This study demonstrated that administering 50,000 IU of Vitamin D biweekly for 8 weeks enhanced insulin metabolism and other lipid profile parameters in infertile women with PCOS who were prospective IVF candidates [54]. Menstrual regularity was observed in 70% of patients who received calcium, Vitamin D, and metformin, while follicular response occurred in 28% of patients; however, no statistically significant difference was noted between the two groups post-therapy. Vitamin D treatment may rectify insufficiency, substantially elevate vitamin levels, and reduce BMI. Moreover, Vitamin D administration may be advantageous for treating patients with PCOS, extending beyond the enhancement of insulin resistance and infertility [55].

Metformin Treatment

The biguanide medicine Metformin, an anti-hyperglycaemic agent, has been widely utilised in infertile women with PCOS. Despite being an authorised prescription for PCOS, metformin has historically been utilised to address T2DM and is among the insulin-sensitizing agents commonly employed in the treatment of PCOS [56]. In women with anovulatory PCOS, metformin use reduces insulin levels, luteinizing hormone (LH) production, and circulating androgen concentrations. Metformin enhances glucose absorption, resulting in reduced insulin production or secretion. This drug's protective benefits encompass the restoration of ovulatory cycles, menstrual cycles, and fertility, as aberrant insulin levels impair the functioning of the hypothalamus-pituitary axis, ovaries, and glucose utilisation in peripheral tissues [57]. The clinical pregnancy rate with metformin was much greater than that of the placebo. Metformin administration to stimulate ovulation in PCOS patients resulted in an increase in both clinical pregnancy rates and ovulation frequency [58].

Selenium

It is a constituent of antioxidant enzymes, including glutathione peroxidase, which assist in neutralising reactive oxygen species and mitigating oxidative stress. Selenium's antioxidant qualities may be advantageous in mitigating oxidative damage. Selenium may contribute to enhanced insulin sensitivity, albeit without a direct hormonal effect. Selenium is recognised for its ability to regulate immunological responses, inflammation, and hormonal equilibrium. Chronic low-grade inflammation is linked to PCOS, and selenium's anti-inflammatory properties may aid in the effective control of PCOS symptoms [59].

Oral Contraceptives: Hormonal contraceptives (including oral contraceptives, patches, or vaginal rings) are the primary therapeutic strategy for monthly irregularities and hirsutism/acne in women with PCOS. Oral contraceptives (OCPs) are an effective therapeutic choice for women who wish to avoid conception. These function by enhancing direct negative feedback on LH secretion, leading to less ovarian androgen production and thereby alleviating hyperandrogenism. They elevate sex hormone-binding globulin from the liver and reduce circulating free androgens. Additional mechanisms via which oral contraceptive pills (OCPs) function encompass the inhibition of peripheral conversion of testosterone to dihydrotestosterone, the binding of dihydrotestosterone to androgen receptors, and the reduction of adrenal androgen output. The combination oral contraceptive pill does not enhance the insulin resistance often associated with hyperandrogenism.

Oral contraceptive pills exacerbate insulin resistance and elevate the risk of inflammatory and coagulatory problems in women with and without polycystic ovary syndrome. Nonetheless, metformin had worse outcomes in the free androgen index, insulin secretion, plasma triglyceride levels, sex hormone-binding globulin (SHBG) levels, and testosterone levels when compared to combined oral contraceptive pills (COCPs), as indicated by a meta-analysis of 36 randomised controlled trials (RCTs) [61]. Moreover, the amalgamation of COCPs with metformin markedly lowered fasting glucose and fasting insulin levels in comparison to COCPs alone [62]. Their effects on women's metabolic profiles are inconsistent due to both absolute and relative contraindications, as well as associated hazards and benefits among the general population. Their advantages are enhanced when used in conjunction with metformin therapy, as per the 2023 International Guidelines[63].

Omega-3 Fatty Acids

Given the evidence supporting the beneficial impact of omega-3 supplementation on inflammation and cardiometabolic changes, and acknowledging that cardiovascular issues typically arise post-40 years in women with PCOS, a universal distribution of omega-3 fatty acids to all PCOS patients, irrespective of age and requirements, appears unwarranted. Omega-3 fatty acids may mitigate the inflammatory condition in women with PCOS by lowering high-sensitivity C-reactive protein (hs-CRP) and elevating adiponectin levels. Consequently, the administration of omega-3 fatty acids should be restricted to women with PCOS who display inflammatory and cardiovascular symptoms, often manifesting between the ages of 40 and 45 years [64][65][66]. Omega-3 fatty acids has a greater caloric value than other dietary supplements, necessitating cautious assessment of their usage in obese or overweight individuals to prevent adverse effects on metabolic changes frequently observed in women with PCOS.

Bariatric/metabolic surgery

It may be seen beneficial for enhancing weight loss, managing hypertension, treating diabetes (both prevention and intervention), addressing hirsutism, regulating menstrual cycles, facilitating ovulation, and improving pregnancy rates in women with PCOS. Bariatric/metabolic surgery for women with PCOS should adhere to recommendations established for the general population. Polycystic Ovary Syndrome (PCOS) is a metabolic disorder that may be regarded as a criterion for bariatric/metabolic surgery at a lower BMI threshold, akin to other metabolic disorders such as diabetes. Women should receive comprehensive guidance regarding the probability of swift fertility restoration and the necessity of adhering to adequate contraception, preferably before undergoing surgery. Contraception should be maintained until a stable weight is attained, typically after one year, even when pregnancy is wanted, to mitigate the heightened risk of growth restriction, preterm, small for gestational age, pregnancy difficulties, and extended hospitalisation of the newborn.

Laparoscopic ovarian drilling: For women experiencing anovulatory infertility unresponsive to pharmacological interventions, laparoscopic ovarian drilling (LOD), a minimally invasive surgical technique, may serve as a viable option for inducing ovulation (evidence-based conditional recommendation, low quality of evidence). The most effective procedure involves executing 5 to 10 holes on the ovarian surface bilaterally, utilising monopolar energy. The predominant mechanism by which LOD facilitates the restoration of ovulatory function is the ablation of androgen-producing tissue, specifically theca cells in the ovary, resulting in decreased ovarian androgen synthesis, diminished peripheral androgen levels, and consequently reduced conversion to oestrogens. A diminished negative feedback from oestrogens on the hypothalamus results in decreased LH levels and elevated FSH levels, hence suitably reinstating follicular stimulation. Within the ovary, the milieu becomes mostly oestrogenic, facilitating follicular maturation and subsequent ovulation.

The surgical technique has several advantages over medical therapy, including a diminished risk of ovarian hyperstimulation syndrome (OHSS) and multiple pregnancies, lower cycle cancellation rates in patients subsequently undergoing in vitro fertilisation (IVF), and consequently reduced direct and indirect expenditures. A Cochrane review by Farquhar et al. revealed no significant difference between laparoscopic ovarian drilling (LOD) and medicinal therapy regarding live birth rates, miscarriage rates, or ovarian hyperstimulation syndrome (OHSS) rates. There are also concerns that this approach may lead to reduced ovarian reserve and the production of periadnexal adhesions. Unilateral drilling is typically recommended, as there is "no evidence of a significant difference in rates of live birth, pregnancy, ovulation, or miscarriage" when compared to bilateral drilling.

Individuals who are overweight or obese face an elevated risk of adverse outcomes and a greater likelihood of developing problems. 10.61 Abu Hashim et al. identified several potential predictors of adverse outcomes, including prolonged infertility, significant hyperandrogenism, elevated AMH levels, and diminished LH levels [69].

Letrozole is regarded as the primary pharmaceutical intervention for ovulation induction in women with PCOS experiencing anovulatory infertility, provided there are no additional infertility causes. A new meta-analysis of clinical studies including women with PCOS assessed the relationship between low-dose aspirin combined with letrozole and reproductive outcomes in this population. The scientists discovered that the incorporation of aspirin with letrozole markedly enhances reproductive outcomes, including an elevated pregnancy rate and a reduced miscarriage rate. The authors requested more validation by multi-center, large-sample, high-quality randomised controlled trials (RCTs). A recent study indicated that the proteomic profile of simple pregnancies with polycystic ovary syndrome (PCOS) resembles that of pregnancies affected by pre-eclampsia. Consequently, women with PCOS may gain advantages from low-dose aspirin consumption during pregnancy to reduce pre-eclampsia and its associated neonatal consequences, such as intrauterine growth restriction, premature delivery, low birth weight, and perinatal mortality. Nonetheless, the advantage requires validation in PCOS.

Clomiphene citrate (CC)

This is the primary treatment for those with irregular or missing ovulation. It exhibits anti-estrogenic properties and inhibits oestradiol receptors in the hypothalamus, resulting in alterations to the pulse frequency of gonadotropin-releasing hormone (GnRH), the secretion of follicle-stimulating hormone (FSH) from the anterior pituitary, and subsequent follicular maturation. A meta-analysis indicated that CC is an efficacious first-line intervention for enhancing pregnancy rates in comparison to placebo. The administration of 50–150 mg of CC daily for five days commences on days 3–5 of spontaneous or provoked bleeding, beginning with the minimum dosage and escalating by 50 mg per day with each cycle. Homburg advised an initial dosage of 100 mg/day commencing on day 4 or 5 and determined that a daily dosage exceeding 150 mg conferred no further benefit. 6 Furthermore, this dosage does not appear to substantially enhance follicular recruitment or the ovulation rate. This treatment protocol minimises the quantity of unnecessary treatment cycles until ovulation is achieved or CC resistance develops. Since roughly 75% of clomiphene citrate (CC) pregnancies transpire within the initial three treatment cycles, a regimen of 3–6 ovulatory cycles is typically adequate to ascertain pregnancy occurrence with CC prior to initiating additional treatment. The likelihood of conception following treatment, if the patient ovulates, is influenced by factors including age. More than 73% of women ovulated, 36% achieved pregnancy, and 29% delivered after six months of CC treatment. Ultrasound is conducted on days 11–14 of the cycle to evaluate endometrial thickness and follicular development, aiding in the determination of the optimal timing for natural intercourse or intrauterine insemination (IUI). This can effectively reduce potentially inappropriate or excessive therapy and mitigate the risk of multiple pregnancies.

Factors contributing to CC resistance encompass obesity, advanced age, heightened blood testosterone levels, and insulin resistance. Approximately 75% of pregnancies following CC treatment transpire within the initial three treatment cycles, with a minority occurring beyond six cycles. Consequently, six ovulation cycles of Clomiphene Citrate are typically adequate before considering more intricate treatments. In conclusion, for patients with PCOS devoid of additional infertility causes, clomiphene citrate should be employed as the primary treatment to enhance reproductive results in women with anovulatory infertility [72].

CONCLUSION

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder affecting women of reproductive age, characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology. Its etiology involves a combination of genetic, hormonal, metabolic, and environmental factors, including insulin resistance, obesity, and chronic low-grade inflammation. PCOS is associated with significant complications such as infertility, type 2 diabetes, cardiovascular diseases, endometrial cancer, and psychological disorders like anxiety and depression. Current treatment strategies focus on symptom management rather than a cure. Lifestyle modifications, including diet and exercise, remain first-line interventions to improve insulin sensitivity and weight management. Pharmacological treatments include oral contraceptives to regulate menstrual cycles, anti-androgens (e.g., spironolactone) for hirsutism and acne, and metformin to address insulin resistance. For infertility, ovulation induction agents like clomiphene citrate and letrozole are commonly used, while assisted reproductive technologies (ART) may be required in resistant cases. Despite advances in understanding PCOS, several challenges remain. The heterogeneity of PCOS makes diagnosis and treatment difficult, with no universal therapeutic approach. Long-term management of metabolic and cardiovascular risks is often overlooked, necessitating a multidisciplinary care model. Additionally, the psychological impact of PCOS is under-addressed, highlighting the need for integrated mental health support.

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