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"The Evaluation and Management of Patients Suffering from Polycystic Ovary Syndrome"

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Abstract :

Anovulation, androgen excess (often ovarian, but also adrenal in origin), and the appearance of polycystic ovaries on ultrasound all describe polycystic ovary syndrome (PCOS), the most common endocrinopathy among adult women in the developed world. Expert-based diagnostic criteria are contested because they fail to take into account the known metabolic abnormalities associated to aberrant insulin action that affect many women with the syndrome. These abnormalities include glucose intolerance, diabetes, and dyslipidemia. The most bothersome symptoms for patients include hirsutism, obesity, infertility, and menstruation abnormalities. Epidemiological research have not shed light on the syndrome's potential long-term effects, such as an elevated risk for cardiovascular events based on risk factor profile. Genetic investigations support the idea that the condition is caused by a complicated genetic disorder, suggesting that its aetiology is multifactorial. Gonadotropin and gonadotropin receptor genes, interestingly, are the ones identified as candidates in many genome-wide association studies that best match into current hypotheses about the pathophysiology. Symptoms are usually treated, and the search for a panacea that corrects reproductive and metabolic problems continues. Hormonal contraception, progestins, and metformin are frequently used for the long-term management of PCOS. Ovulation induction therapies, which may include medications like letrozole or clomiphene or gonadotropin therapy, are at the centre of infertility treatment. Hormonal contraceptives and anti-androgens are frequently used together in the treatment of hirsutism. Obese women with PCOS may benefit from weight loss for infertility therapy and long-term management.

- **Introduction:**

Ovarian hyperandrogenism, ovulatory dysfunction, and polycystic ovaries are the hallmarks of polycystic ovary syndrome (PCOS). In the industrialised world, it may be the most common form of female endocrinopathy. However, its pathophysiology and origin are both open to debate, suggesting that it constitutes a diverse illness. Oligo-ovulation (which can lead to oligomenorrhea), infertility, acne, and hirsutism are all symptoms of PCOS in young women. Long-term treatment must also take into account the increased risk of diabetes and cardiovascular risk factors that are a consequence of the condition. A multifaceted strategy has emerged to combat these various stigmas, with most treatments focusing on a specific symptom or set of symptoms (Rodgers,2016). The prevalence of polycystic ovarian syndrome (PCOS) among reproductive-aged women varies from 8 to 13 percent, depending on the population investigated and the classifications employed. PCOS is multifaceted, affecting a person's reproductive system, metabolism, and mental health. Women all around the world have reported delayed diagnosis and dissatisfaction with care due to discrepancies in clinical practise in the examination and management of PCOS. Inconsistent advice for both doctors and women results from the current guidelines' lack of scope, lack of adherence to best practise in creation, lack of consumer involvement, and/or antiquated nature(Gibson-Helm & Dokras,2017).

Genetics, the environment, and inter-racial marriage all play a role in the rising prevalence of polycystic ovary syndrome (PCOS), although the disease is more accurately understood as a combination of insulin resistance, hyperandrogenism, and follicular abnormalities . Type 2 diabetes mellitus, glucose intolerance, hyperinsulinemia, cardiovascular diseases, and hypertension are all closely linked to the onset of PCOS(Sidra et al ,2019). More than 60% of individuals with PCOS, including obese and non-obese populations, have been documented to

have insulin resistance, and up to 10% of women with PCOS may acquire type 2 diabetes by the age of 40. Patients with polycystic ovary syndrome (PCOS) often have increased levels of both luteinizing hormone (LH) and anti-Müllerian hormone (AMH)(Dokras,2017).

- **Clinical features and diagnostic criteria:**

PCOS can have a wide range of clinical manifestations. Symptoms of PCOS include irregular periods, clinical signs of hyperandrogenism, and infertility. Oligomenorrhea, amenorrhea, and protracted irregular menstrual bleeding are common menstrual abnormalities in PCOS. But 30% of PCOS women will have regular periods. Oligomenorrheic women are more likely to have PCOS than are amenorrheic women (85%-90% vs. 30%-40%) (Unluhizarci ,2012).

Androgen excess affects more than 80% of women, and PCOS is the leading cause. Seventy percent or more of PCOS women will experience hirsutism, a frequent clinical manifestation of hyperandrogenism. The severity of hirsutism is determined using a modified Ferriman-Gallwey score. The upper lip, chin/face, chest, back, belly, arms, and thighs are the seven areas where hair growth can be measured with this instrument. Terminal hair development is given a score of 0 if present and a score of 4 if present in abundance. Hirsutism is indicated by a sum score of 8 or higher. Ultrasound diagnoses polycystic ovaries in over 90% of women with hirsutism who menstruate regularly. 9 Moreover, PCOS affects 50% of women, typically resulting in a less pronounced pattern of facial hair growth. The presence of acne can also be indicative of hyperandrogenism, however it is less common in PCOS and less specific than hirsutism. Acne affects between 15–30% of PCOS-diagnosed adult women. Since 5-reductase is expressed differently in the sebaceous gland and the hair follicle, the latter produces more dihydrotestosterone, which may explain why hirsutism is more common than acne. Over forty percent of women with severe acne who were evaluated were found to have polycystic ovary

syndrome. Acne patients who are female should be questioned about their menstrual history and checked for other indicators of hyperandrogenism, according to some doctors (Sirmans,2014).

Around 40% of PCOS-affected women also experience infertility. Anovulatory infertility is most commonly brought on by polycystic ovary syndrome (PCOS). Infertile women who are anovulatory typically have PCOS. There is no abnormality in the number of primordial follicles in PCOS women, but there is a dramatic rise in the number of primary and secondary follicles. However, once follicles attain a diameter of 4-8 mm, follicular growth becomes stopped as a result of disruptions in components essential in normal follicular development. Ovulation does not occur because a dominant follicle does not form. In addition, between 42 and 73 percent of pregnancies affected by PCOS end in a spontaneous abortion (Fauser,2012).

The National Institute of Health's National Institute of Child Health and Human Disease (NIH/NICHD), the European Society of Human Reproduction and Embryology/American Society of Reproductive Medicine (ESHRE/ASRM), and the Androgen Excess and PCOS Society have all proposed diagnostic criteria for PCOS (Legro et al ,2014).

There is some agreement between the various groups' criteria, but there are also significant discrepancies. Congenital adrenal hyperplasia, nonclassic adrenal hyperplasia, Cushing syndrome, androgen-secreting tumour, idiopathic hyperandrogenism, idiopathic hirsutism, hyperprolactinemia, and thyroid problems are all considered to be excluding conditions in each issuing group's criteria for PCOS (Lujan et al ,2013). The existence of polycystic ovaries (PCO) alone was not deemed satisfactory by any group because 20%-30% of normally normal women exhibit evidence of numerous cysts on their ovaries. Hyperandrogenism, as defined by the National Institute of Child Health and Human Development (NICHD) and the Androgen Excess Society, requires patients to exhibit symptoms like hirsutism and have hyperandrogenemia, which is

characterised by increased levels of free testosterone, decreased levels of SHBG (sex hormone-binding globulin), an increased free testosterone index, or an increased dehydroepiandrosterone sulphate. However, PCOS can be diagnosed according to ESHRE/ASRM (Rotterdam) criteria even in the absence of hyperandrogenemia and clinical hyperandrogenism. As defined by the Rotterdam criteria, women with ovulatory failure and polycystic ovaries are diagnosed with PCOS. The criteria also differ in their respective treatment of oligomenorrhea and amenorrhea. Women with regular menstrual cycles may still be diagnosed with PCOS if they have PCO in addition to hyperandrogenism or hyperandrogenemia, as stated by the Rotterdam criteria. Even in women who have normal menstrual flow, ovulatory dysfunction may exist at the subclinical level. But according to the National Institute of Child Health and Human Development (NIH/NICHD), PCOS cannot be diagnosed in women who have regular menstrual cycles but have subclinical ovulatory dysfunction (Lujan et al ,2013) .

Accurately describing polycystic ovarian morphology is essential for making a diagnosis of PCOS according to the Rotterdam and AES criteria. If a woman has 12 or more follicles measuring between 2 and 9 mm in diameter, or if her ovarian volume is larger than 10 cm3, she is considered to have polycystic ovary syndrome, according to the criteria provided by the Rotterdam consensus group. This solitary ovarian appearance adequately characterises polycystic ovary. However, considerable improvements in ultrasound image technology have occurred since then, allowing for the detection of smaller follicles and a higher resolution overall. This has led to demands for a reevaluation of the diagnostic criteria for polycystic ovary syndrome. Using three-dimensional transvaginal ultrasonography, counted the number of follicles in each ovary and the most follicles that could fit in a single sonographic plane in ten patients with PCOS and 29 normoandrogenic ovulatory controls. The median FNPO of 20.1 was 100% specific and 70% sensitive in detecting

PCO. PCO was detected with 100% specificity and 90% sensitivity when a total of ten follicles were seen in a single sonographic plane. Two-dimensional transvaginal ultrasonography found that an ovarian volume of 13.1 cm3 or less was predictive of polycystic ovary syndrome with a sensitivity of 0.5. Dewailly et al. quantified the ovarian volume and the total number of follicles smaller than 10 mm in diameter using two-dimensional transvaginal ultrasonography. Predicting polycystic ovary syndrome with a cutoff follicle count of 19 had an 81% sensitivity and a 92% specificity. A threshold of 7 cm3 ovarian volume for PCO diagnosis was associated with an 87% sensitivity and an 89% specificity (Teede et al ,2013).

- **Incidence of PCOS :**

Different diagnostic criteria lead to different estimates of PCOS prevalence. Approximately 25-30% of women of childbearing age have polycystic ovaries, as detected by ultrasonography. This means that the great majority of women who have polycystic ovaries do not actually have the syndrome. About 7% of reproductive-aged women have inexplicable hyperandrogenic chronic anovulation (i.e., NIH criteria). The extent to which minority groups are disproportionately afflicted by polycystic ovary syndrome is a topic of controversy(Day et al ,2015)

n. Other research has demonstrated that Latinx, Native American, and African-American groups are disproportionately affected by insulin resistance and type 2 diabetes. For PCOS women, however, there is weaker proof of this. No significant differences in PCOS prevalence or PCOS stigmata, such as hirsutism or elevated circulating androgen levels, were found between white and black women in the best study of an unselected population in the United States, which involved women applying for jobs at an academic medical centre. The incidence of polycystic ovary syndrome (PCOS) rises by 50 percent when using the broader Rotterdam criteria rather than the more stringent NIH criteria, with the AES criteria yielding an intermediate result (Day et al ,2015).

Overweight and obesity are both connected to PCOS, and the global obesity epidemic has been linked to a rise in PCOS prevalence. there are still significant variations in the prevalence of obesity and morbid obesity among women with PCOS by place of origin. There appears to be a lower prevalence of obesity and especially severe obesity among women with PCOS in Europe and Asia. According to the available research, the United States has the greatest rate of both extreme obesity and PCOS. Large, randomised, multi-center trials of women with PCOS and infertility consistently show a mean body mass index of 35. Obesity has been linked to polycystic ovary syndrome (PCOS), however the exact relationship between the two remains controversial. Mendelian randomization methodology used in a European GWAS revealed an association between increased BMI and risk (Hayes et al ,2015).

- **Clinical Presentation:**

Since its initial description, polycystic ovary syndrome (PCOS) has been associated with menstruation problems (from amenorrhea to dysfunctional uterine haemorrhage) and infertility in women. Even though obesity is now much more prevalent in the public, the collection of presenting symptoms. from the 1960s is still applicable today. PCOS typically manifests at or after menarche for two reasons: the focus on menstrual history and the complaint of androgen excess (unusual in children). However, there is some evidence to suggest that girls who experience pubarche too early are at a higher risk of having PCOS later in puberty, despite the fact that the phenotypic in pubertal and pre-pubertal girls is still up for debate (Bazarganipour et al ,2013). Hyperinsulinemia and increased levels of DHEAS are found in girls who develop pubertal symptoms early. Premature pubarche is just a factor in a tiny percentage of women with polycystic ovary syndrome. The rate of premature pubescence in Denmark is estimated to be 22–23 cases per 10,000 females, or 0.0002 percent, based on data from a national register of all children in the

country. Women with PCOS appear to experience a return to normal menstrual cycles and reduced levels of androgens when they enter the perimenopausal and menopausal stages of their reproductive lives. There is no way to tell if these will ever return to normal, although evidence suggests that modest elevations may be hereditary and persist; for example, mothers of women with PCOS have increased testosterone levels compared to controls (Legro,2015).

Women with PCOS typically present with a skin problem, especially one caused by peripheral androgen excess, such as hirsutism, acne, or even androgenic alopecia. A centripetal distribution is often seen in cases of obesity. A high waist circumference (more than 88 centimetres) is diagnostic. Occurrences of oligomenorrhea and hirsutism may precede the development of obesity, prompting some to suspect an acquired form of polycystic ovary syndrome. The body mass index (BMI) should be measured at each visit for all women with PCOS. Many women with PCOS have low self-esteem as a result of being overweight, having disfiguring hirsutism, and being unable to conceive a child (Teede et al ,2018).

- **sequelae of PCOS :**

In spite of the fact that the endocrine and reproductive symptoms of the condition might become better with age, the accompanying metabolic abnormalities, most notably glucose intolerance, might actually get worse. The most prevalent complications of polycystic ovary syndrome (PCOS), such as infertility caused by ovulatory dysfunction, anomalies of the pilosebaceous unit, certain gynaecological malignancies, type 2 and gestational diabetes, and cardiovascular disease, will now be discussed (CVD).

- Infertility as a Result of Chronic Anovulation Women who have polycystic ovary syndrome (PCOS) are not often sterile but rather subfertile as a result of the irregularity and unpredictability of their menstrual cycles. Despite the fact that many women now seek therapy

earlier on in their reproductive lifetimes, there is a possibility that certain women with PCOS may have a tendency to conceive later in life when ovulatory function improves . Ovulation induction can be one of the most challenging medical procedures, and women with polycystic ovary syndrome (PCOS) are typically among the most challenging patients to treat. Ovulation induction with clomiphene citrate is ineffective or ineffective for many women who have polycystic ovary syndrome (PCOS). They are at an elevated risk for ovarian hyperstimulation syndrome and may have an incorrect or excessive reaction to the administration of human menopausal gonadotropins (menotropins) (OHSS) (Heijnen et al ,2006). Ovarian hyperstimulation syndrome (OHSS) is a phenomenon characterised by huge enlargement of the ovaries, the development of fast and symptomatic ascites, intravascular contraction, hypercoagulability, and malfunction of systemic organs. Because of the potential risk to one's life, its avoidance is strongly recommended. A lower likelihood of acquiring the syndrome may be associated with rising obesity rates. Ovarian hyperstimulation has been recorded in women with PCOS who conceived a singleton pregnancy on their own, as well as in those who took clomiphene or pulsatile GnRH after the treatment with menotropins. However, these issues often arise after therapy with menotropins (Heijnen et al ,2006).

- Skin Diseases Abnormalities of the pilosebaceous unit are the primary cause of skin disorders in women who have polycystic ovary syndrome (PCOS). Increased systemic and local synthesis of androgens (see above) have been linked to the development of PCOS-related symptoms such as hirsutism, acne, and androgenic alopecia. These symptoms are characterised by the activation of aberrant development of the pilosebaceous unit. Although insulin is necessary for the proliferation of hair follicles in vitro, it is not known whether the hyperinsulinemia that is associated with PCOS actually drives the

transformation of fine vellus hair into thick, black terminal hair, which is required for the development of hirsutism. Acne during the peri-pubertal phase, hirsutism during the young adult years, and androgenic alopecia during the mature adult years are the typical progressions of abnormalities that occur in the pilosebaceous unit throughout the ontogeny of abnormalities in the pilosebaceous unit. Androgenic alopecia is fortunately uncommon in women who have PCOS, and the aetiology of this condition is likewise somewhat complicated (Tasali et al ,2011). It would appear that the same elements that cause follicular atresia in the scalp are the same factors that cause terminal midline hair to grow in lower body locations. Treatments that are intended for hirsutism are, for the most part, applicable to androgenic alopecia as well (i.e., androgen suppression and androgen antagonism). On the other hand, local vasodilators that are applied in the form of a crème or lotion, such as minoxidil, have been demonstrated to be useful for treating androgenic alopecia in both males and females, whereas there is no evidence that they have any positive effect on hirsutism (Barry et al ,2014).

- Sleep Apnea In women who have polycystic ovary syndrome (PCOS), there is an increased risk for sleep apnea as well as other sleep disorders, such as sleep disordered breathing, according to multiple studies. This is significant because sleep apnea is not as common in women, particularly premenopausal women. There is a correlation between hyperandrogenism and insulin resistance in PCOS, which has been linked to an increased risk for these illnesses in women who have PCOS. In women who have polycystic ovary syndrome (PCOS), insufficient sleep may contribute to a vicious metabolic cycle that worsens insulin resistance and glucose tolerance. PCOS is a predictor of morbidity and mortality in patients undergoing bypass surgery; therefore, it should be considered in

women undergoing bariatric surgery. Although it is too early to recommend universal screening in obese women with PCOS, it should be considered in women undergoing bariatric surgery. Women who suffer from sleep difficulties frequently report feeling sleepy during the day and exhausted after sleeping, and they may also snore. It is interesting to note that the conventional treatment for sleep apnea, which is known as continuous positive airway pressure (CPAP), has been proven to increase insulin sensitivity, decrease sympathetic output, and reduce diastolic blood pressure in women who also have PCOS and sleep apnea (Ramezani-Binabaj et al ,2014) .

- fatty liver disease not caused by alcohol use (NAFLD). This condition, which is characterised by fatty infiltration of the liver, is not caused by excessive consumption of alcohol but rather by insulin resistance. Patients who are afflicted with the condition could exhibit no symptoms at all or only moderate, non-specific symptoms like weariness or malaise. In most cases, this condition is accompanied by abnormally high levels of serum liver function tests, most frequently transaminases. Steatosis can be seen on a liver ultrasound, but the definitive way to diagnose liver disease is by a liver biopsy, which also reveals indications of inflammation and fibrosis. It is possible for this condition to improve with insulin sensitising treatment and weight loss (Lerchbaum& Obermayer-Pietsch, 2013). There is still disagreement over the extent to which the disease is prevalent among women who have PCOS. A recent meta-analysis found that women who have PCOS have an almost four-fold greater incidence of NAFLD compared to those who were in the control group. A recent multi-center experiment that evaluated over 1,000 women with PCOS found that only a small fraction (5%) had elevated liver transaminases. While some reports have shown an increased prevalence, this finding contradicts the findings of the trial. This

prevalence is comparable to that which was discovered in the general population of the United States of America by the NHANES survey. At this point in time, it is likely not required to perform routine screening, and doing so is not encouraged by practise standards (Celik et al ,2014).

- **Current treatment approach for PCOS :**

There is currently no known treatment for PCOS. Weight loss, a low-carbohydrate diet, and regular exercise are all part of the usual treatment for polycystic ovary syndrome (PCOS). Infertility, hirsutism, menstrual abnormalities, and obesity are frequently treated medical concerns in cases of polycystic ovary syndrome (PCOS). Few treatments exist that are effective for a wide range of signs and symptoms. The combination of infertility and hirsutism is the hardest to treat because oral contraceptives prevent ovulation and anti-androgens are teratogenic for the developing male embryo. Because of their mutual incompatibility, these treatments cannot be used to combat hirsutism and infertility simultaneously. Infertility caused by anovulation or oligo-ovulation I and symptoms related to elevated levels of androgens (ii) that require ongoing therapy (Li et al ,2015). An Overview of the Management of Infertility Caused by Anovulation. Couples experiencing anovulatory infertility should be screened for additional causes of infertility before beginning treatment. Ten percent of men with PCOS had severe oligospermia at the same time, and nearly five percent of women with PCOS had bilateral blockage of the fallopian tubes or some uterine component, according to a large multi-center trial. Screening for these conditions before starting treatment is warranted due to the obvious impact they have on the course of care. When it comes to ovulation induction for women with PCOS, there is currently no evidence-based framework to help guide initial and subsequent choices. Preconceptual counselling should stress the importance of lifestyle, with a focus on weight loss and exercise for overweight women, quitting smoking, and

cutting back on alcohol, as recommended at a conference sponsored by the American Society for Reproductive Medicine and the European Society for Human Reproduction and Embryology (Merz et al ,2016).

General Information about PCOS Upkeep over the Long Term. To far, no cure for PCOS has been discovered, therefore treatment focuses on managing symptoms. The major presenting problem is typically prioritised in treatment. However, hirsutism, oligomenorrhea, and obesity are generally the most noticeable signs. This is when it could make sense to zero in on a single metabolic indicator as the starting point for treatment. Glucose intolerance is one potential criteria to employ in selecting early treatment because it is the biggest risk factor for diabetes and an independent risk factor for cardiovascular events in women. The discovery of a potential first-line strategy that enables selection of medicines that improve the PCOS triad is a major step forward in the treatment of this disorder. Depending on how well the initial treatment goes over, additional hirsutism and/or oligomenorrhea targeted medicines may be added. If the patient wants to prevent pregnancy, contraception is a logical option to consider (Hart & Doherty ,2015).

- **Treatment for PCOS-related symptoms:**

- Hirsutism :

1. Spironolactone, metformin, and eflornithine are considered first-line drugs for the treatment of hirsutism. Because of their mild androgenic effects, oral contraceptives including norgestimate, desogestrel, and drospirenone are frequently used to treat hirsutism (Alchami , 2015).
2. Oral contraceptives are commonly used to treat menstrual problems. Treatment for menstrual abnormalities was successful with spironolactone, acarbose, rosiglitazone, and metformin (Glintborg et al ,2006).

3. Metformin is the drug of choice because it reduces insulin resistance and glucose intolerance in women with polycystic ovary syndrome. Furthermore, rosiglitazone and pioglitazone have both been reported to be helpful in treating PCOS (Glintborg et al ,2006).

Negative consequences from taking so many different drugs are a reality for some women. Potential side effects of clomiphene citrate include blurred vision, sweating, abdominal pain, depression, irritability, breast tenderness, dizziness, and nausea. currently To take clomiphene citrate, you must first have a valid prescription valid for 6 months. Clomiphene citrate and letrozole do not have any anti-oestrogenic effects on the endometrium or the cervical mucus. Ovulatory disruption leading to polymenorrhea is a possible side effect of spironolactone, along with polydipsia, polyuria, nausea, headache, lethargy, and gastritis. When taken together, clomiphene citrate and metformin might cause nausea, vomiting, and gastrointestinal problems. Metformin must be used indefinitely to control PCOS, and stopping the medicine after only three months can undo any progress made (Pachiappan et al , 2017).

Due to the potential for PCOS treatment to require a long-term commitment, these side effects are particularly concerning, and a plant-based drug's minimal bad effects may make it the best choice for the disease's management. The following is a list of plant-based ingredients that have been linked to positive effects in the treatment of polycystic ovary syndrome (PCOS) (Hewlings , 2017).

- **Conclusion:**

PCOS is a diverse condition with a variety of possible diagnoses due to its complexity. Oligomenorrhea, which is indicative of oligo-ovulation, polycystic ovaries, and hyperandrogenism are the primary diagnostic criteria for polycystic ovary syndrome. Hyperandrogenism can be clinical (i.e., hirsutism) or biochemical (i.e., high free testosterone or free androgen index). There is a growing consensus that the Rotterdam criteria should serve as the primary diagnostic criteria.

Women who have PCOS typically have insulin resistance, obesity, and an increased likelihood of developing diabetes as well as an unfavourable cardiovascular risk profile. Treatment typically focuses on alleviating specific symptoms, such as those associated with infertility, obesity, hirsutism, and so on. There are just a few treatments that can alleviate all of the syndrome's signs and symptoms. It is hoped that a more in-depth understanding of the genetics and pathophysiology of the disease may lead to the development of treatments that are more targeted.

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