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A REVIEW: CONCISE INSIGHT INTO POLYCYSTIC OVARIAN SYNDROME

PREVALENCE, PATHOPHYSIOLOGY, DIAGNOSIS, DIETARY MANAGEMENT INCLUDING TREATMENT

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Abstract: The metabolic disorder known as polycystic ovarian syndrome affects reproduction worldwide and is linked to unfavourable results. It causes an overabundance of male hormones in the body. Cysts are liquid-filled sacs. PCOS symptoms were classified by the National Institutes of Health as oligomenorrhea or amenorrhoea along with clinical or laboratory confirmation of hyperandrogenaemia. Menstrual dysfunction, subfertility, endometrial hyperplasia, and oligo-ovulation, which presents as seborrhea, are associated with the most severe forms of resistance to insulin and metabolic comorbidities. The Androgen Excess Society in 2006 and Rotterdams (2003) have both reported differing rates of prevalence. The interplay between metabolic problems and reproductive failure shapes the diverse pathophysiology of PCOS. The goal of treating PCOS patients should be to achieve fertility, or in the case of nonfertile individuals, to address or mitigate the psychological effects of excess androgen, irregular menstruation, and the possibility of endometrial hyperplasia.

Index Terms – Amenorrhoea, hyperplasia, Androgen Excess Society, Oligo-ovulation.

I. INTRODUCTION

Polycystic ovary syndrome (PCOS) is a syndrome of ovarian dysfunction that is characterized by endocrine, metabolic and genetic disorders, chronic absence of ovulation of polycystic ovary (Hart *et al.*, 2004) (Abasian *et al.*, 2018). The clinical and biochemical features are heterogeneous, and there has been much debate as to whether it represents a single disorder or several (Franks 1995) (Abasian *et al.*, 2018). Its cardinal features include clinical ones (menstrual disorders, hirsutism, acne, baldness, and infertility), changes in endocrine hormones (increased levels of androgen, estrogen, and prolactin and decreased level of progesterone), and metabolic disorders (insulin resistance, diabetes, dyslipidemia, and type 2 diabetes) (Abasian *et al.*, 2018). Although PCOS is the most common endocrine disturbance to affect women of reproductive age (Hart *et al.*, 2004), its definition has been controversial in disciplines as diverse as internal medicine, gynaecology, and psychiatry and natural history remain unclear. Therefore, polycystic ovary syndrome is a persisting challenge for clinical and basic research scientists who try to elucidate its origins and distinguish primary pathological changes from secondary environmental disruptions (Norman *et al.*, 2007).

1.1 DEFINITION OF POLYCYSTIC OVARIAN SYNDROME

PCOS was first described in 1935 by Stein and Leventhal as the combination of hirsutism (a condition of male-pattern terminal hair growth in women), amenorrhoea (absence of menstruation), chronic anovulation and infertility, obesity and enlarged cystic ovaries (Morreale 2018). Seminal contributions to our understanding of PCOS pathogenesis began with the 1958 report that urinary LH was elevated by bioassay in the 4 cases studied. The 1970 documentation by RIA that serum LH and the ratio of LH to FSH were typically high led both to the adoption of altered gonadotropin secretion as an alternative diagnostic tool and to a focus of research on the putative neuroendocrine genesis of the syndrome. Shortly thereafter, plasma free testosterone was recognized as a marker for hyperandrogenism in hirsute amenorrheic women (Robert *et al.*, 2016). However, it was not until 1990 that the WHO included 'E28.2 Polycystic ovarian syndrome' — with sclerocystic ovary syndrome and Stein–Leventhal syndrome as synonyms — among the disorders of ovarian dysfunction included in the International Classification of Diseases, 10th revision (ICD10) (Morreale 2018).

Definition of PCOS reflects increasing awareness that the clinical expression of PCOS might be broader than that defined by the 1990 NIH/NICHHD criteria. This definition relied on a combination of oligomenorrhoea or amenorrhoea and clinical or biochemical evidence of hyperandrogenaemia (in the absence of non-classical adrenal hyperplasia and hyperprolactinemia and thyroid dysfunction) (Hart *et al.*, 2004).

European Society of Human Reproduction and Embryology and the American Society of Reproductive Medicine in 2003 — the so-called Rotterdam criteria — has not been universally accepted, and three definitions for PCOS remain valid at present. The Rotterdam definition is the most widely used PCOS classification, and it is currently supported by most scientific societies and health authorities. The definition proposes that PCOS can be diagnosed in any woman presenting with at least two of the three following characteristics: clinical and/or biochemical hyperandrogenism, ovulatory dysfunction and PCOM. By contrast, the 2006 Androgen Excess and PCOS Society (AE–PCOS) Position Statement requires the presence of hyperandrogenism, which must be accompanied by evidence of ovarian dysfunction in the form of ovulatory dysfunction and/or PCOM. Finally, the National Institute of Child Health and Human Development has an older definition that requires the presence of both hyperandrogenism and ovulatory dysfunction but does not consider ovarian morphology. This definition represents the most severe phenotype of the PCOS spectrum, and it is included within both the Rotterdam and AE–PCOS definitions. Of note, these definitions equally consider clinical and/or biochemical hyperandrogenism, even though there is a definite lack of convincing evidence to show that these two forms of androgen excess have the same health consequences for patients. The three definitions require exclusion of specific disorders that might have signs and symptoms that overlap with those of PCOS, such as non-classic congenital hyperplasia, hyperprolactinaemia, thyroid dysfunction, hypercortisolism and androgen-secreting tumours (Morreale 2018).

Two international consensus conferences have developed adult diagnostic criteria that widen the definition beyond NIH criteria by incorporating the presence of PCOM, defined by consensus, as a diagnostic criterion for PCOS (Table 1)

Table 1: Diagnostic Criteria for PCOS

Adult Diagnostic Criteria (Rotterdam) (Otherwise unexplained alternative phenotypes)			
1. Phenotype 1 (classic PCOS)	2. Phenotype 2 (Essential NIH Criteria)	3. Phenotype 3 (ovulatory PCOS)	4. Phenotype 4 (nonhyperandrogenic PCOS)
a. Clinical &/or biochemical evidence of hyperandrogenism b. Evidence of oligo-anovulation c. Ultrasonographic evidence of a polycystic ovary	a. Clinical and/or biochemical evidence of hyperandrogenism b. Evidence of oligo-anovulation	a. Clinical and/or biochemical evidence of hyperandrogenism b. Ultrasonographic evidence of a polycystic ovary.	a. Evidence of oligo-anovulation b. Ultrasonographic evidence of a polycystic ovary.

Adolescent Diagnostic Criteria (Otherwise unexplained combination of)	
1. Abnormal uterine bleeding pattern	2. Evidence of hyperandrogenism
a. Abnormal for age or gynecologic age b. Persistent symptoms for 1–2 y	a. Persistent testosterone elevation above adult norms in a reliable reference laboratory is the best evidence b. Moderate-severe hirsutism is clinical evidence of hyperandrogenism

An independent panel reviewed the evidence through 2012 in an international workshop and recommended that Rotterdam criteria be adopted with specific identification of phenotype, of which there are 4, listed next in order of decreasing clinical severity, which corresponds to decreasing specificity of the milder phenotypes (Rosenfield RL *et al.*, 2016).

II Clinical features

Polycystic ovary syndrome (PCOS) may present with a variety of clinical manifestations, which may differ according to ethnic, racial, and environmental factors, and the co-existing presence of, among other factors, obesity and insulin resistance. However, the most commonly associated clinical abnormalities observed in PCOS are hyperandrogenism, oligomenorrhea, and polycystic ovaries, although the specific phenotypes considered to represent the disorder may vary according to the definition used. The onset and progression of hyperandrogenic signs and symptoms, menstrual dysfunction and irregularity, symptoms of obstructive sleep apnea, and the family history, unwanted hair growth, acne or scalp hair loss, or unexplained weight gain or overweight (obese) . Another frequent presenting complaint of PCOS may be infertility, possibly associated with recurrent first trimester miscarriages and history of premature adrenarche or early pubarche may also be elicited as well as a history of low birthweight. Alternatively, the rapid development of symptoms, including hirsutism, oligo-amenorrhea, severe acne and alopecia, increased muscularity, and clitoromegaly, is indicative of a virilizing syndrome, most commonly caused by an androgen-producing neoplasm (Futterweit *et al.*, 2007).

2.1 Prevalence and Phenotypes

The prevalence of polycystic ovarian syndrome is generally thought to be between 3% and 10% but it is widely unknown for specific subpopulations based on geographical location and race/ethnicity (wolf *et al.*, 2018). The prevalence of PCOS varies depending on the diagnostic criteria, phenotypes, and populations studied. Bozdag et al reviewed a total of 55 prevalence studies. According to the diagnostic criteria of National Institutes of Health, Rotterdam, and AE-PCOS Society, the rates of PCOS prevalence were 6, 10 and 10%, respectively. The range for prevalence on Rotterdam criteria was 8 to 13%. The Rotterdam criteria have four phenotypes (Table 2).

The classic phenotype women present with hyperandrogenism and oligomenorrhea with (A) or without (B) PCO on ultrasound. In the "ovulatory phenotype," women have hyperandrogenism and PCO (C). In the "non-hyperandrogenic phenotype," there is oligomenorrhea and PCO, without overt hyperandrogenism (D).

Table 2: Polycystic ovary syndrome phenotypes

Phenotype			
A	Androgen excess	Ovulatory dysfunction	Polycystic ovarian morphology
B	Androgen excess	Ovulatory dysfunction	---
C	Androgen excess	Polycystic ovarian morphology	---
D	Ovulatory dysfunction	Polycystic ovarian morphology	---

Prevalence of phenotypes is variable, as this depends greatly on how the population was identified. In an Indian population, among all PCOS women, 56% presented with phenotype A, 15% with phenotype B, 11% with phenotype C, and 18% with phenotype D. Phenotypes A and B were seen more in obese women, with more hyperandrogenemia, insulin resistance, and worse cardiometabolic profile. Metabolic syndrome

prevalence was lowest in phenotype D.15 However in other studies, these differences were not as clear. The guideline has emphasized the need for defining phenotypes in research, but the clinical relevance of this remains somewhat unclear at present (Neven *et al.*, 2018).

III Diagnosis

The diagnosis of polycystic ovary syndrome is usually made on the basis of a combination of clinical, ultrasonographic, and biochemical criteria. A woman presenting with oligomenorrhea is likely to have the polycystic ovary syndrome if she has one or more of these three features: polycystic ovaries on ultrasonography, hirsutism, and hyperandrogenemia (*i.e.*, serum testosterone concentrations of 85 to 150 ng per deciliter [3 to 5 nmol per liter) points to a benign, ovarian cause of the hirsutism, whether or not the term "polycystic ovary syndrome" is used.. Many women with the syndrome have hypersecretion of luteinizing hormone, although normal serum concentrations of luteinizing hormone do not rule out the diagnosis.

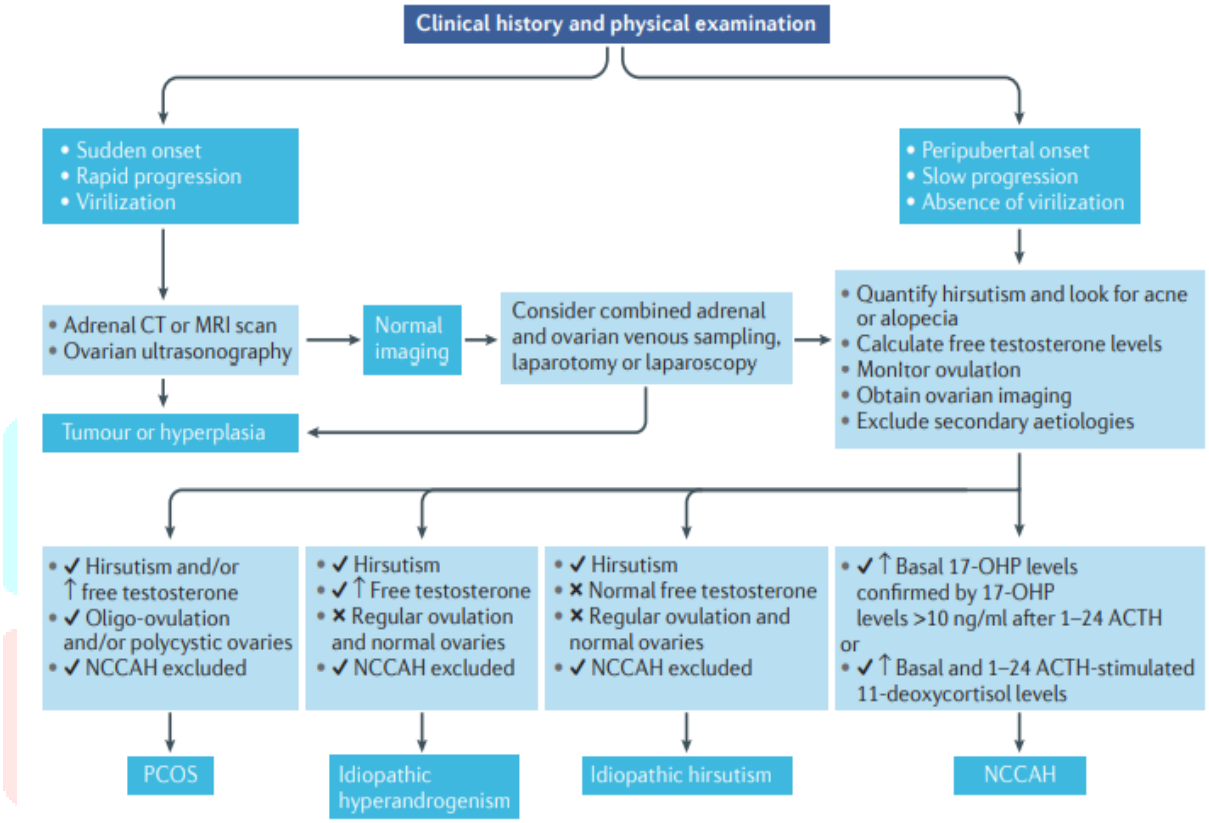

Figure 1: Algorithm for the aetiological diagnosis of women thought to have PCOS.

Non-classic congenital adrenal hyperplasia (NCCAH) or hyperprolactinaemia. Androgen Excess and Polycystic Ovary Syndrome Society (AE–PCOS) 1–24 ACTH, cosyntropin; 17OHP, 17-hydroxyprogesterone.

In PCOS patients the primary diagnosis is of pituitary or adrenal diseases — for example, hyperprolactinemia, acromegaly, and classic or nonclassic congenital adrenal hyperplasia. The polycystic ovary syndrome can be distinguished from late-onset (nonclassic) congenital adrenal hyperplasia due to 21-hydroxylase deficiency by measuring the 17a-hydroxyprogesterone response to corticotropin, but it is arguable whether such a test should be performed routinely in populations in which the frequency of congenital adrenal hyperplasia is low or in women whose serum testosterone concentrations are less than 150 ng per decilitre. The differential diagnosis of hirsutism includes androgen-secreting tumors of the ovary or adrenal gland.

Although rare, it is important to consider this diagnosis in patients with a short history of hirsutism, those with severe hirsutism, and those whose serum testosterone concentrations are greater than 200 ng per deciliter (7 nmol per liter). The presence of acanthosis nigricans in a patient with marked virilization is a useful clinical marker, since this suggests the polycystic ovary syndrome and is not a feature of androgen-secreting tumors (Franks 1995). Determining whether a patient has PCOS must be a straightforward process (Figure 1), as the criteria used in all current classifications are the same, and it is only the combination of criteria that is disputed. However, the accuracy of the diagnosis of PCOS is equal to the accuracy of the evaluation methods used to assess the individual criteria, and no efforts should be spared to use the most appropriate methods available (Morreale 2018).

II. Pathophysiology and Etiology of PCOS

The cause of PCOS has not yet been definitely determined (Figure 2); however, it is mainly characterized by hyperandrogenism, infertility, lack of ovulation, increased level of LH, increased insulin resistance, decreased sex hormone-binding globulin (SHBG), and hirsutism which visualized as well as diagnosed by ultrasonography and laboratory tests. Because of disrupted secretion rate and metabolism of androgens and estrogens in women with PCOS, the serum concentrations of androgens such as testosterone, androstenedione, and dehydroepiandrosterone are most probably high in such women.

In addition, the incidence of certain complications such as environmental insulin resistance and hyperinsulinemia is very likely. Such complications lead to obesity at different degrees. Insulin resistance can occur due to impaired signaling pathway of insulin receptor. With increase in insulin (Insulin resistance), the effect of gonadotropins on ovarian function increases which results in increased LH/FSH, and adiponectin decreases in patients with PCOS due to insulin resistance. These hormone changes in the theca cells and granulosa cells (GCs) cause increase in the synthesis of androgens and decrease in the synthesis of estradiol, and stops the maturation of follicles, leading to impaired ovulation and therefore development of PCOS (Abasian *et al.*, 2018).

The exact cause of PCOS isn't known. Excess insulin is one factor that may be involved. The hormone insulin, which is made in the pancreas, enables cells to utilise sugar, the body's main source of energy. Your blood sugar levels may increase and your body may produce more insulin if your cells become less responsive to the effects of insulin. Extra insulin may boost testosterone production, which could make ovulation challenging. Low-grade inflammation: This phrase refers to the compounds that white blood cells produce to fight illness. According to research, polycystic ovaries in women with PCOS are stimulated to generate androgens, which can cause issues with the heart and blood vessels. Heredity: According to research, PCOS may be caused by specific genes. Too much androgen: Acne and hirsutism are caused by the ovaries' unusually high androgen production

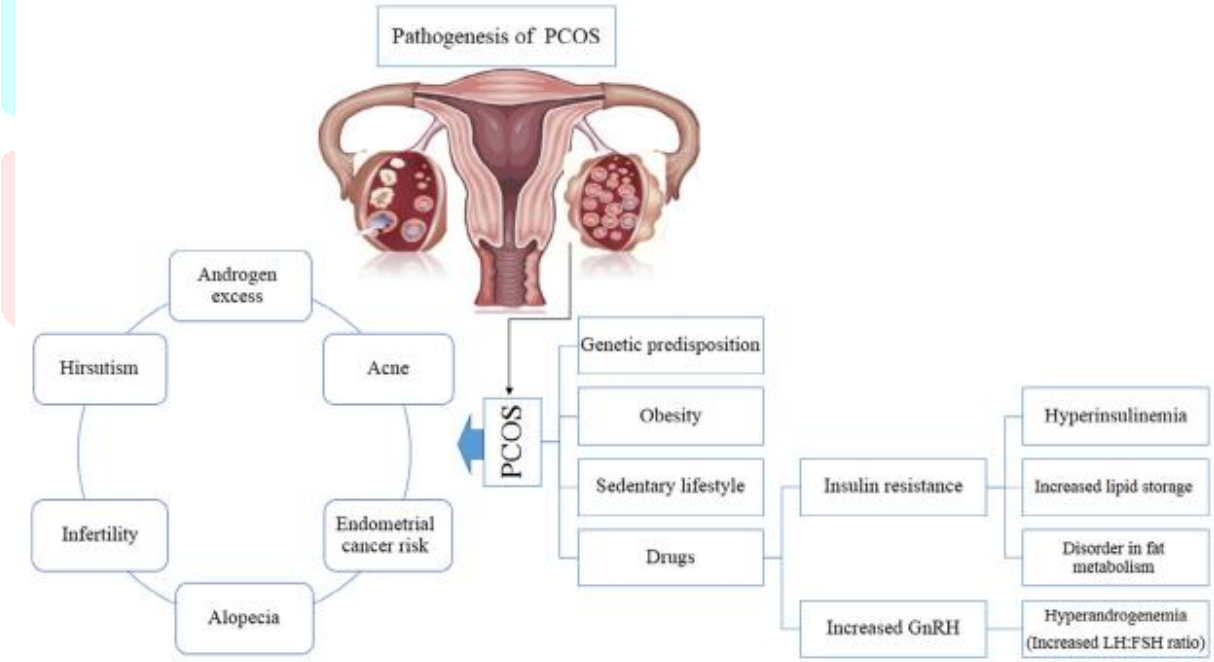

Figure 2: Pathogenic factors in PCOS

- **Environmental factors :** It includes physical exercise, lifestyle, and food may vary widely according to the population (Escobar-Morreale *et.al.,* 2005). Environmental factors also include endocrine-disrupting chemicals and glycotoxins that may cause genetic variance and disruption of the metabolic and reproductive pathways, which can develop PCOS phenotypes and related complications (Kandarakis *et.al.,* 2016).
- **PCOS and Hyperandrogenism:** Impaired folliculogenesis is the result of surplus androgens that disrupt normal androgen synthesis. The excess androgens promote the development of primordial follicles and increase in the antral follicles at the early gonadotropin stage (Ehrmann *et.al.,* 2016). The release of gonadotropin hormones from the pituitary is triggered by GnRH production from the brain.
- While follicular stimulating hormone simultaneously operates on the FSH receptor in the ovarian granulosa cells to convert androgens to estrogens, which stimulate follicle growth, luteinizing

hormone stimulates the LH receptor to enhance androgen synthesis in ovarian theca cells (Ashraf *et.al.,* 2019).The dysregulation of the neuroendocrine system is known to cause an imbalance in the hypothalamic-pituitary-ovarian axis, which then leads in an excess of gonadotropin.The rise in the GnRH promotes the production of LH over FSH, resulting in a marked hormonal increase in the LH:FSH ratio in PCOS (Walters *et.al.,* 2018, Tsutsumi and Webster *et.al.,* 2009).

- **Insulin Resistance And Type 2 Diabetes:** Hyperinsulinemia is the root cause of excess androgens as insulin directly stimulates the action of LH and raise the GnRH indirectly (Barber *et.al.,* 2016). The primary circulatory protein controlling the testosterone levels, sex hormone binding globulin (SHBG) is decreased by insulin. Therefore a lower SHBG would lead to a higher level of free androgens which cause clinical symptoms such hirsutism, alopecia, and acne (Rojas *et.al.,* 2014). Insulin resistance can cause dyslipidemia and the patients with PCOS are at high risk for cardiovascular disease and diabetes (Rocha *et.al.,* 2019) Numerous investigations demonstrated that reducing insulin resistance will eventually result in less excess androgens and an improvement in the disease (Ashraf *et.al.,* 2019, Baillargeon *et.al.,* 2004).
- **Obesity and PCOS:** Obesity is associated with hyperinsulinemia, which raises the lipid profile and is associated with glucose intolerance in PCOS.Obesity is linked to hyperinsulinemia which further increases the lipid profile, glucose intolerance in PCOS patients. Obesity augments the androgen production by stimulating LH, which in turn leads to hyper androgenism (Glueck *et.al.,* 2019).Obese PCOS women's neuroendocrine and reproductive health are directly impacted by leptin, an adipokine that regulates appetite (Rojas *et.al.,* 2014, Barber *et.al.,* 2006). Furthermore, hyperleptinemia may hinder ovarian follicular growth (Barber *et.al.,* 2006). Therefore, reducing visceral fat would regulate glucose levels, lipolysis, appetite, and SHBG levels, which in turn would regulate the ovarian androgen response

IV TREATMENT OF PCOS

Treatment of polycystic ovary syndrome targets the reproductive, cutaneous, metabolic, and psychological complications (Setji et.al., 2006). PCOS is treated by

1. Lifestyle intervention
2. Pharmacological treatment
3. Long term management
4. Invitro fertilization
5. Surgical procedure

4.1. Lifestyle Interventions: Treatment for PCOS usually initiates with a series of lifestyle modifications such as diet, weight loss, and exercise. Losing weight is one of the most effective measures to regulate the menstrual cycle and improve the symptoms of PCOS. In low glycemic diets (LGD), the glycemic index (GI) is used to determine which foods have the least significant effect on blood sugar levels; thus, LGD may help weight loss (Saadati *et al.,* 2021).

Lifestyle interventions such as diet and exercise are first line treatment for women with polycystic ovary syndrome, particularly if they are overweight. Several nonrandomized trials have shown that a reduction in body weight through diet and exercise improves insulin sensitivity and ovulation rate. In other populations, weight loss of 5%-7% decreases the conversion from impaired glucose tolerance to type 2 diabetes by 58% over a 3-year period. Taken together, these data support lifestyle interventions in this high-risk population.

Dietary changes in PCOS management: Some of the dietary changes are as folows

4.1.1 A low glycemic index (low GI) diet:

It gets most carbohydrates from fruits, vegetables, and whole grains helps regulate the menstrual cycle better than a regular weight loss diet. Low glycemic index foods may be helpful for people with insulin resistance as they are digested more slowly than high GI foods. This slow digestion results in a gradual rise in blood sugar levels, consequently improving the reaction to insulin levels in the body and preventing a sudden rise in insulin. The concept of the glycemic index (GI) was created to quantify the glycemic responses stimulated by carbohydrates in different foods. GI is an important tool that influences our food choices and used to classify the foods on the basis of carbohydrate content. Low GI foods are associated with a lower postprandial blood glucose level, lower insulin demand, reduction in blood lipid level, increasing fermentation in the colon and improving satiety (Kaur *et al.,* 2021)

4.1.2 Magnesium intake:

Magnesium is a mineral found in a wide variety of foods and is the fourth most abundant mineral in the body. As with all minerals, magnesium helps the body to function optimally. Magnesium is one of the cations found in the human body that takes part in energy transformations and determines the proper course of hormonal reactions and insulin secretion. The secretion of insulin is initiated by the influx of Ca2+, which is competitively inhibited by extracellular Mg2+. This may explain the inverse correlation between serum Mg2 + concentration and serum-insulin concentration (Pokorska et al., 2021). Almonds, cashews, spinach, and bananas are PCOS-friendly foods rich in magnesium.

4.1.3 Intake of fibre foods

Lower dietary fiber intake is indicated to be associated with the metabolic and hormonal disturbances in PCOS. Short-chain fatty acids (SCFAs), which are key microbial metabolites produced in the colon through fermentation of dietary fiber by gut microbes, are famous for possessing functional roles in regulating host metabolism, immune system, and cell proliferation. A decrease in fiber intake could possibly affect the production of metabolites, especially SCFAs, and finally influence overall health and well-being. Considering that PCOS women consume less dietary fiber, whether there is a reduction in SCFA production remains unclear. Furthermore, whether increasing SCFA level by modulating dietary fiber intake or through dietary supplementation has a beneficial effect on PCOS warrants (Leung et al., 2021)

4.1.4 Inositol:

The inositol stereoisomers, myo-inositol (MI) and D-chiro-inositol (DCI), are hexahydroxy cyclohexanes present in fruits and beans, the inositols are incorporated into cell membranes as phosphatidyl-MI, which is a precursor of inositol triphosphate (InsP3). InsP3 is a second messenger for many hormones including insulin and follicle-stimulating hormone (FSH). Defects in this pathway can lead to impaired insulin signaling and cause insulin resistance (Kalra *et al*., 2016). MI treatment improved ovarian function and fertility, decreased the severity of hyperandrogenism including acne and hirsutism, positively affected metabolic aspects, and modulated various hormonal parameters deeply involved in the reproductive axis function and ovulation (Kamenov *et al.*, 2020). Grains are among the foods high in inositol. Note that inositol occurs in whole grains and not processed, refined grains. Legumes and sprouts are also considered as foods high in inositol. Vegetables, such as bell peppers, tomatoes, potatoes, and asparagus, along with green leafy vegetables, are also good sources of Inositol. Nuts and seeds also contain a good amount of inositol.

4.2 Pharmacological treatment:

a) First line treatment:

- **Metformin**: Metformin decreases blood glucose levels by decreasing hepatic glucose production (also called gluconeogenesis), decreasing the intestinal absorption of glucose, and increasing insulin sensitivity by increasing peripheral glucose uptake and utilization
  Pharmacokinetics: Metformin is slowly absorbed and has a 50–60% oral bioavailability if used while fasting. Peak plasma concentrations (Cmax) are acquired after administering immediaterelease metformin within 1-3 hours and after taking extended-release versions between 4 and 8 hours.
  Uses: Metformin is a medicine used to treat type 2 diabetes, and to help prevent type 2 diabetes if you're at high risk of developing it. Metformin is used when treating polycystic ovary syndrome (PCOS), although it's not officially approved for PCOS.
- **Thiazolodinediones:** Thiazolidinediones (TZDs) are substances that increase insulin sensitivity in important organs by acting on intracellular metabolic pathways to improve insulin action. Adiponectin levels, hepatic gluconeogenesis, and insulin-dependent glucose absorption in muscle and fat are all increased by TZDs.. Adiponectin, a cytokine secreted by fat tissue, increases insulin sensitivity, and fatty acid oxidation increases with TZD therapy
  Pharmacokinetics: Thiazolidinediones are rapidly absorbed and reach peak concentrations within a few hours. Although steady-state is often reached in one week, it could take 4–12 weeks for the full benefit to become apparent due to the significance of fat redistribution. In the bloodstream, rosiglitazone and pioglitazone are highly protein-bound, primarily to albumin. The thiazolidinediones have not been associated with any notable medication interactions, although it should be noted that when used with sulfonylureas, hypoglycemia may occur as a result of the combination of increased insulin sensitivity (from the thiazolidinediones) and increased insulin production (sulfonylureas).

Uses: Drugs called thiazolidinediones are used to manage and treat type 2 diabetes mellitus.

- **Clomiphene citrate**: Clomiphene (Clomid, Serophene) is an oral anti-estrogen, may add metformin to help induce ovulation. In most women with PCOS and anovulation, this oral oestrogen antagonist elevates circulating FSH concentrations and triggers follicular growth. Clomiphene is a selective oestrogen receptor modulator that has both oestrogenic and antioestrogenic properties. Clomiphene citrate binds to selective estrogen receptor modulator (SERM) found in the hypothalamus, blocks the negative feedback of oestrogen at the level of hypothalamus and the pituitary. This binding facilitates the stimulation and production of GnRH, which leads to the release of the gonadotropins FSH and LH. Estradiol rises about 2 to 3 times its normal level when clomiphene citrate treatment is suppressed to a decrease in GnRH. The ovulation-inducing LH peak is triggered by the elevation in estradiol. The first dosage is 25–50 mg per day for five days.. Therapy can be monitored by oestrogen levels, follicular ultrasound examination and luteal progesterone level (>20nmol/L). Increased weight and high androgen levels are linked to lack of response.

b) Second line treatment:

Gonadotrophin treatment: Ovulation induction with gonadotrophins such FSH has been effective for at least three decades, but it requires knowledge and expertise to prevent multiple pregnancies and ovarian hyperstimulation syndrome. Patients start on low- dose recombinant FSH administered subcutaneously. Ultrasound examination, frequently linked with oestradiol measurement, can be used to monitor ovarian response.When a follicle grows to a size of 16 to 20 mm, human chorionic gonadotrophin is administered. Any more than two follicles of an appropriate size give the risk of multiple pregnancies. Multiple gonadotrophin cycles may be required to achieve pregnancy, but this approach is preferable before more invasive procedures, such as in-vitro fertilisation.

43. Long-term management: Women with PCOS require ongoing surveillance to detect impaired glucose tolerance, hyperlipidaemia, endometrial hyperplasia and consequent complications. Obese women, in particular, require regular (possibly annual) glucose tolerance testing because of the potential for rapid progression from normal to impaired glucose tolerance and diabetes (Norman *et.al.*, 2001). To prevent the difficulties related with the metabolic syndrome, several researchers have suggested using Metformin as a precaution in youngsters and older women. At this point, which is probably premature to take this action, so it is not recommended. Advice about improved exercise and diet is more rational, given the abundant data on the role of lifestyle change in preventing and treating problems of glucose metabolism**.**

4.4 In-vitro fertilisation: Provided there is no problem other than anovulation, this has little place in the management of infertility resulting from PCOS. Ovulation induction by a skilled reproductive endocrinologist is preferable to in-vitro fertilization because of the risks of hyperstimulation and multiple pregnancies with the latter procedure

4.5. Surgical Treatment:

Surgery to the ovaries: Wedge resection of the ovaries has been abandoned because of concerns about pelvic adhesions, another cause of sub fertility, and loss of valuable ovarian tissue. Recent reviews comparing laser drilling with clomiphene citrate and gonadotrophins showed equivalent in the studies evaluated. Ovarian led to improvement or laser drilling has been employed in recent years may seem to be good results (Farquhar et.al., 2003). Similar to wedge resection, this technique can lead to pelvic adhesions. If the ovaries are determined to be polycystic incidentally during regular laparoscopy, destructive surgery on the ovary should only be used after significant discussion with the patient

V CONCLUSION

Dietary components like low fiber, low magnesium, low vitamin A and high glycemic load, may contribute to IR/HI and obesity. In addition, low fiber intake may contribute to hyperandrogenemia. Life style intervention is primary pathway for management of PCOS

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