A review on Polycystic Ovary Syndrome

Krishna Chhaniyara, Dr. Vipulkumar Gajera, Dr. Tanvi Desai, Dhara Parekh

Abstract— More than 1 out of 10 women worldwide are diagnosed with polycystic ovary syndrome (PCOS), the leading cause of female reproductive and metabolic dysfunction. Despite its high prevalence, PCOS and its accompanying morbidities are likely underdiagnosed. Although it has been intensively researched, the underlying cause(s) of PCOS have yet to be defined. But, as per the research done so far, Polycystic Ovary Syndrome (PCOS), the most common endocrinopathy in women is characterized by polycystic ovaries, chronic anovulation and hyperandrogenism, and many more. These disturbances are a consequence of PCOS’s complex aetiology. PCOS is mainly related to women with obesity; however, there are many PCOS lean patients too. This review will explain from the beginning, starting with; what it is, then its aetiology, pathophysiology, diagnosis, and how to manage PCOS, in which we particularly focus on the diet, which should be followed during this condition to overcome from it and on the other hand, medications used are Metformin, Oral contraceptives, and Antiandrogens. However, the treatment for PCOS is mainly symptomatic and involves lifestyle interventions, which is quite challenging and current interventions are not able to deal with the outcomes of this syndrome. Thus, this article will shed a light on the PCOS’ essential data, which should be noteworthy enough, for a reader. Importantly, the major focus is on the factors causing this syndrome and the various feasible treatment options available for it, with a particular diet need to be followed.

Index Terms— Polycystic Ovary Syndrome, PCOS, Reproductive health, Hormonal imbalance, Metabolic disorder, Obesity, Diet, Medicines, Metformin, Holistic Yoga Approach

1. Introduction

Before we get into all the details of PCOS, we should understand what it means. Poly Cystic Ovarian Syndrome is a disorder of hormones that is very commonly seen in women of reproductive age. Poly Cystic means multiple cysts. Women who have PCOS have less frequent or prolonged menstrual periods or would have excessive male hormones. All women have two ovaries that alternately release an egg every month. PCOS occurs when the ovaries fail to release eggs regularly due to the formation of many small collections of fluids called follicles on them. These fluids/cysts happen when the ovaries release a lot of immature/partly mature eggs which become cysts after some time. The left ovary has multiple cysts and is enlarged due to it as compared to a healthy cyst-free ovary on the right.

Poly cystic Ovary Syndrome (PCOS) is still an under-recognized, under-diagnosed, and under-studied disease, affecting vast numbers of the female population around the globe, especially in developing countries. In 1935, Stein and Leventhal first discovered Polycystic Ovarian Syndrome in females. Therefore, the disease is also known as Stein and Leventhal syndrome. Women with PCOS remain undiagnosed in preliminary care. Therefore, it becomes a healthcare-related economic burden. Further, well-designed prospective studies are still required to predict the long-term risk of developing PCOS-associated problems like type2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD). [1] The syndrome is heterogeneous as regards its clinical presentation varying between amenorrhea/oligomenorrhea, hirsutism, abnormal uterine bleeding, infertility, and metabolic problems including obesity. Women often consult clinicians including gynecologists, endocrinologists, and dermatologists considering the diversity in clinical presentations with varying phenotypes. [2] Hirsutism, menstrual irregularities, and infertility are considered the most distressing symptoms experienced by women with PCOS. These are accountable for major causes of depression, anxiety, and low self-esteem in women. Due to the complex pathogenesis of PCOS, the treatments are individualized depending upon prevailing signs and symptoms and are very rarely mono-therapeutic. Several adjunctive interventions have been put forward for the management and treatment of PCOS. Lifestyle intervention is regarded as the cornerstone for the management of PCOS. [3] For infertility treatment, lifestyle modifications are combined with ovulation induction agents like clomiphene citrate and aromatase inhibitors (Letrozole). For Insulin resistance and hyperandrogenic conditions insulin sensitizers and antiandrogens are given alone or in combination. Newer insulin sensitizers have been tried in
PCOS which include Myoinositols, GLP-1 agonists, DDP-4 inhibitors, and SGLT2. Oral Contraceptives are considered the first-line treatment in the management of menstrual abnormalities and hyperandrogenic symptoms in PCOS. [4] Statins and bromocriptine have also been added as treatment options in PCOS for hyperandrogenic and dyslipidemia conditions. Of late, Vitamin D alone or in combination with calcium supplementation has shown promising results in improving PCOS conditions.

From the feminine perspective, hirsutism associated with PCOS is considered the most distressing symptom. The problem is not just the unwanted hair growth, but the psychological distress, social stigma, and emotional impact on the female identity. In order to improve the physical appearance, various methods like plucking, shaving, and waxing have been adopted to hide this condition temporarily. However, to accomplish the permanent destruction of hair follicles, various techniques like electrolysis and laser hair removal methods have been adopted. Another technique called acupuncture has also gained popularity in terms of managing PCOS. The use of Traditional/Folk medicine has become a trending option nowadays, as patients believe that homemade remedies can cure the disease with fewer side effects. [5]

So, the aim to review this topic is to provide all the essential information in one place including symptoms, aetiology, pathophysiology, treatment & other necessary details.

II. Symptoms

Polycystic ovarian women show symptoms such as menstrual abnormalities, oligo amenorrhea, or amenorrhea. The general symptoms of PCOS are anovulation or oligo ovulation. The excessive production of androgens is only due to cysts which further leads to virilization or the expression of masculine characters in females. As a result, polycystic ovarian syndrome causes the appearance of a range of male-like characteristics or hyperandrogenism. Physical signs of hyperandrogenism are obesity, abdominal and subcutaneous fat, hirsutism, alopecia, clitoromegaly, deep voice, seborrhoea, acne, etc. Accepting these morphological signs, changes in metabolic profile take place. Patients with hyperandrogenism have a low amount of Serum Sex Hormone-Binding Globulin (SHBG), particularly in association with PCOS. [6]

The major symptom of PCOS is insulin resistance. The elevation in the level of insulin leads to hyperinsulinemia and causes diabetes mellitus. Central adiposity or the deposition of fat in the abdominal region is also due to the high level of insulin. In most females with a polycystic ovarian syndrome, the BMI is 30 or higher than 30. Excepting that, CVDs, hypertension, dyslipidemia, etc. are metabolic disorders of a polycystic ovarian syndrome. [7] Healthy women's blood pressure is 120 and above 80 or less. Women with PCOS are always more prone to develop early arrival cardiovascular diseases. The various symptoms are present in patients with polycystic ovarian syndrome such as sugar craving, recurrent urination, the delayed healing process, exhaustion, distorted vision, sensation, mood swings anxiety, depression, etc. The irregular urinary and bowel movements are also due to the pressing of large cysts against the rectum or bladder. [8] Uterine cancer in females may also be due to polycystic ovarian syndrome, as there is an existence of a high amount of estradiol and lack of progesterone and the ovarian disturbances elevates the threat of endometrial hyperplasia. Because of the disturbed hormonal conditions in polycystic ovarian syndrome, there is a development of light and brown patches on the skin, this condition is known as Acanthosis Nigerians. Various body parts which are more prone to this skin pigmentation are the skin of the neck or armpits, the skin of the thighs, and the breasts. Skin marks also emerged in these areas. Actually, this dark pigmentation acts as a cutaneous indicator of insulin resistance. [9, 10]
Aetiology / Risk Factors

The aetiology is unknown. Genetic factors may play a part, but the exact mechanisms are unclear. Two studies found some evidence of familial aggregation of hyperandrogenaemia (with or without oligo menorrhea) in first-degree relatives of women with PCOS. [11, 12] In the first study, 22% of sisters of women with PCOS fulfilled the diagnostic criteria for PCOS. [11] In the second study, of the 78 mothers and 50 sisters evaluated clinically, 19 (24%) mothers and 16 (32%) sisters had PCOS. [12] The diagnosis excludes secondary causes, such as androgen-producing neoplasm, hyperprolactinemia, and adult-onset congenital adrenal hyperplasia. It is characterized by irregular menstrual cycles, scanty or absent menses, multiple small cysts on the ovaries (polycystic ovaries), mild hirsutism, and infertility. Many women also have insulin resistance, acne, and weight gain. [13] Until recently, there was no overall consensus on the criteria for diagnosing PCOS. In some studies, it has been diagnosed based on the ultrasound findings of polycystic ovaries rather than on clinical criteria. An international consensus definition of PCOS has now been published, which defines PCOS as at least two of the following criteria: reduced or no ovulation; clinical and/or biochemical signs of excessive secretion of androgens; and/or polycystic ovaries (the presence of at least 12 follicles measuring 2–9 mm in diameter, an ovarian volume in excess of 10 mL, or both). [14]

Pathophysiology

As mentioned in the introductory part of the review, PCOS is still an understudied disorder, and a multifaceted syndrome; though certain hormones, genes, and environmental stressors interact with each other.

Hormones

Gonadotropins like; LH & FSH hormones, Estrogen, Progesterone, Testosterone is there, which plays a key role in the pathogenesis of PCOS.

Environmental stressors

Prenatal exposure to androgens and obesity have been considered the main contributing factors. The susceptibility to the polycystic ovarian syndrome is given by various genetic factors and the syndrome will develop only in the presence of a specific environment. The exposure of fetal to maternal androgen in excess amounts is considered to contribute to inducing the PCOS in a fetus. Another cause of various diseases including PCOS condition is oxidative stress. Nowadays antioxidants are used widely as ingredients in their dietary supplements. Due to this, a shift has been found toward the use of herbal and ayurvedic products. Plants mainly contain various bioactive components which might be helpful to cure various diseases such as PCOS. [15]

Genetic Factors

On the basis of the existence of familial clustering, there are facts of a genetic component. The studies based on twins showed a twofold elevated concordance of a polycystic ovarian syndrome in genetically identical twins as compared to non-identical twins. [16] Notwithstanding genes related to the synthesis and metabolism of testosterone and insulin, the way in which polycystic ovary syndrome is inherited remains unclear. [17] Hypothetical contribution of environmental, epigenetic, and genetic factors in the pathophysiology of PCOS. PCOS is a heterogeneous endocrine disorder and its pathogenesis is poorly understood. Current evidence supports gene-environment interactions and epigenetic regulation in the origins of PCOS. The inherited genetic component appears to span all organ systems and physiological functions, with epigenetics capable of modifying the expression patterns of inherited genes. Environmental elements can influence all developmental components by impacting organ systems, physiological function, and epigenetic regulation, with population-specific environmental elements thought to bring about ethnic differences in PCOS sub-phenotypes. While substantial gaps in knowledge still exist, further insights into our understanding of
genetic and developmental contributions to the aetiology of PCOS will significantly improve our ability to diagnose, treat, and prevent PCOS in the future. [18]

Figure 4 Factors contributing to PCOS

V. Diagnostic Criteria For PCOS

Hyperandrogenism and hyperandrogenemia together form a key PCOS diagnostic feature exhibited by > 80% of women with PCOS. Clinical hyperandrogenism is defined by a modified Ferryman Gallwey score (mFG) ≥ 4 to 6, indicating hirsutism. [19] Biochemical hyperandrogenemia in women with PCOS includes elevated circulating levels of T, as well as calculated bioavailable free (unbound) T and free androgen index (FAI), elevated circulating levels of androstenedione and elevated dehydroepiandrosterone sulfate (DHEA-S). Insufficient precision, sensitivity, and specificity of methods used to measure circulating T, androstenedione, and DHEA-S, and also estrogens, by liquid chromatography-tandem mass spectrometry versus assays based on antibody crossreactivity, make comparisons difficult to interpret between various studies (clinical or animal models), particularly since there are no trustworthy cut-off levels for biochemical hyperandrogenemia.

VI. Morphology

Polycystic ovarian morphology (PCOM) is defined as the presence of more than 20 follicles measuring 2 to 9 mm in diameter per human ovary and/or an increased ovarian volume of ≥ 10 cm³. [20] With PCOM, the number of follicles 2 to 5 mm in diameter positively correlates with serum androgen levels, while the number of follicles 6 to 9 mm in diameter negatively correlates with fasting serum insulin and testosterone levels, as well as body mass index (BMI), suggesting that ovarian hyperandrogenism promotes excessive early follicular growth that does not progress to the dominant stage due to hyperinsulinemia and/or androgen excess. [19] These ovarian characteristics distinguish PCOM from other forms of polyfollicular ovarian morphology, which can be a normal stage of development in adolescence or can accompany other forms of ovarian dysfunction. Large, cystic ovarian follicles are therefore not typical of PCOM. PCOM is frequently observed in normal women, and several factors such as pharmacological treatment may affect ovarian size and morphology. [21, 22] Isolated PCOM without other diagnostic criteria is therefore not indicative of PCOS. Based on general population data, periods of irregular cycles in women with PCOS, defined as > 35 or < 21 days that persist 2 or more years post menarche, are likely to indicate oligo-anovulation. With increasing adolescent gynecologic age, therefore, fewer pubertal women experience cycles exceeding 45 days, while adult women over 40 and with PCOS can exhibit more frequent ovulatory menstrual cycles. [20]
VII. Special Age Group Consideration

Adolescence, the period of time between 10 and 19 years of age and the time of pubertal maturation, represents a distinct dilemma in the diagnosis of PCOS. The diagnosis in adolescence is challenged by the overlap of normal pubertal physiology changes and those that mimic adult diagnostic criteria for PCOS, namely irregular menstrual cycles and multi-follicular ovaries. [23, 24] Additionally, the time from menarche to full maturation of the reproductive axis can be variable post-menarche, which may bridge young adulthood. [25] Since there is evidence for the underpinnings of PCOS presenting in adolescence and the normal pubertal overlap, there is the risk of both underdiagnoses [26] and that diagnosis, without adequate support for the disease. As such, it is recommended that the diagnosis of PCOS not be made early in the post-menarchal timeframe. The recommendation for diagnosis in adolescence cannot depend on pelvic ultrasound findings given the increased overlap with normal ovarian findings in this age group and instead is based on irregular menses and hyperandrogenism. Care should be taken when using biochemical evidence of hyperandrogenism to establish a normative range for the assay used in this population. AMH is also unhelpful in distinguishing PCOS in this age group. In adolescents, levels are high and overlap considerably between adolescents with and without diagnostic features of PCOS. [27] Menstrual cycles may not establish a regular pattern until >2 years post-menarche. [28] In a recent study of 16-year-old adolescents, the majority had regular cycles within 3 years post-menarche. [29] Therefore, the diagnosis should not be made within 2 years of menarche to allow for this maturation. There is a recommendation regarding adolescents who are not yet at the developmental stage for full endorsement of a PCOS diagnosis, but who demonstrate concerning features like persistent irregular menses or clinical androgen concerns requiring clinical intervention, that they are considered “at risk for PCOS.” There may therefore be utility in reinvestigating the possibility of PCOS in the future. It is then recommended that further evaluation of androgens and consideration for an ultrasound at the age of peripubertal or adult female rodents, or (3) 2 or more PCOS-like traits generated by non-PCOS-like equivalents of the Rotterdam criteria. Such models are contributing immensely to our molecular understanding of PCOS. Animal models allow highly invasive investigative procedures that are otherwise unethical in humans. Indeed, a fundamental understanding of a human disorder is often only identified following insightful revelations from customized animal models. For example, estrogen resistance was considered incompatible with life until the first estrogen receptor knockout mouse was reported [38], a finding subsequently confirmed in humans. Further elucidation of PCOS etiopathogenesis utilizing animal models is imperative if we are to develop more effective strategies to manage and potentially cure PCOS.

VIII. Animal Models Of PCOS

Evolutionarily conserved mammalian physiological systems enable the use of experimentally manipulated or naturally occurring animal models to provide biological and clinically relevant insight into PCOS etiopathogenesis. Animal models allow highly invasive investigative procedures that are otherwise unethical in humans. Indeed, a fundamental understanding of a human disorder is often only identified following insightful revelations from customized animal models. For example, estrogen resistance was considered incompatible with life until the first estrogen receptor knockout mouse was reported [38], a finding subsequently confirmed in humans. Further elucidation of PCOS etiopathogenesis utilizing animal models is imperative if we are to develop more effective strategies to manage and potentially cure PCOS.

What is the relevant animal PCOS model?

Animal models of relevance to PCOS must, by necessity, have comparability to women with PCOS by exhibiting 2 or more PCOS-like equivalents of the Rotterdam criteria. Such models stand in contrast to exhibiting: (1) Only a single PCOS-like trait, such as T-treated neonatal rats, (2) 2 or more PCOS-like traits alongside PCOS endocrine-mimics (including hyperprolactinemia and hypogonadotrophic amenorrhea), such as DHEA-treated per pubertal or adult female rodents, or (3) 2 or more PCOS-like traits generated by non-PCOS-like mechanisms, (such as testis Leydig cell-typical HSD1B3 contributing to ovarian theca cell hyperandrogenism) as found in estrogen receptor or aromatase knock-out mice. Here, a clear distinction is made between such animal models with potentially limited mechanistic relevance for PCOS [38], where genetically modified mice, that are themselves not PCOS-like models, have been combined with a rodent PCOS-like model and have clearly demonstrated their relevance towards PCOS mechanistic understanding. These latter animal models comprise per pubertal dihydrotestosterone (DHT)-induced PCOS-like mice combined with female mice genetically manipulated, including those with whole body or organ/cell-specific gene knockout of androgen receptors (AR). [39] Such models are contributing immensely to our molecular understanding, as some are unresponsive to androgen programming of a PCOS-like adult phenotype, hence demonstrating the vital contribution of AR either during development and/or in a single organ system as the molecular foundation on which prenatal PCOS-like programming and the Do HAD hypothesis relevant to PCOS are built.

IX. Consequences

What is known

Obesity / Metabolic Disorder

PCOS is associated with an increased risk of metabolic complications starting from a young age. These comorbidities include traditional cardiovascular disease (CVD) risk factors such as obesity, impaired glucose tolerance, type 2 diabetes (DM), dyslipidemia, and hypertension. Obesity is one of the most common concerns expressed in surveys of patients with PCOS. Depending on the ethnicity and study population assessed, the obesity rate varies from 50% to 80%. According to an examination of high-quality studies in a large meta-analysis, the risk of obesity in women with PCOS was reported to be 4-fold higher compared with controls and also higher in white women compared with Asian women. Importantly, women with PCOS have been shown to present with long-term overweight or obesity, with the onset of BMI trajectory deviation occurring as
early as age 5. [41] Evidence from cross-sectional studies suggests that the risk of overweight/obesity persists beyond the fourth decade of life [42] and a few longitudinal studies also suggest an increase in weight with age. [43] The increased preference for abdominal fat deposition, seen primarily in the hyperandrogenic phenotype, further predisposes this population to other cardio metabolic complications. [44] The risk of impaired glucose tolerance is 3-fold higher with PCOS, independent of BMI, and highest in women living in Asia and in North and South America. [45] Although the risk of DM is also increased in this reproductive-age population, there are mixed data regarding these findings independent of weight. In women over age 40, a few longitudinal studies and other cross-sectional studies indicate an increased risk of type 2 DM independent of BMI. [42] In adolescents with PCOS, there are only a few small studies examining the risk of DM, and these show an overall low prevalence. When examining the differences based on PCOS phenotype, a large cross-sectional study showed a similar risk of DM in all 4 phenotypes. [46] Dyslipidemia, reflected by high triglycerides and low high-density lipoprotein cholesterol, is the most common metabolic abnormality detected in PCOS. [47] Some studies have performed deep lipid phenotyping and demonstrated high low-density lipoprotein cholesterol levels, an increase in atherogenic lipoproteins, and a decrease in high-density lipoprotein cholesterol efflux capacity, indicating increased CVD risk. [48] When examining the risk in different age groups, there are few studies in adolescents and those in older women show a higher prevalence of dyslipidemia in the hyperandrogenic phenotype. [49] The association between hypertension and PCOS is mixed. Most studies do not demonstrate a higher risk of hypertension independent of BMI, although longitudinal data demonstrate elevated blood pressure even in lean women with PCOS. [50] The few studies on adolescents and older women do not show significant differences compared with control groups. [51] Given that most of the data on metabolic risk is derived from cross-sectional studies, the long-term significance of mild to moderately abnormal values for blood pressure measurements and serum lipids is not clear. Another approach is to evaluate the prevalence of metabolic syndrome as it assesses early evidence of dyslipidemia, hypertension, glucose intolerance, and obesity as a composite score and may predict long-term risk of DM and CVD. Reproductive-age women with PCOS have a 2-fold increased risk of metabolic syndrome [52], with a higher risk in the hyperandrogenic phenotype. [53] More importantly, in adolescents with PCOS, the risk of metabolic syndrome is at least 2-fold higher than in girls without PCOS. [54]

Reproductive / Obstetrics

Women with PCOS are at an increased risk of endometrial hyperplasia and infertility related to anovulation. Premenopausal women with PCOS may have a 4-fold increased risk of endometrial cancer. [55] For women with PCOS who are seeking pregnancy, the ovulation induction agent letrozole is associated with higher live birth rates compared with clomiphene citrate. [56] The use of metformin in conjunction with these medications may improve the ovulation rate in a subpopulation of obese women. Depending on the ethnicity and study population assessed (e.g. clinical cohort’s vs population-based studies) the obesity rate varies from 50% to 80%. [57] Metformin, on the other hand, has not been shown to reduce the risk of gestational diabetes (GDM); thus, its use should be limited to prior to pregnancy for metabolic management and to facilitate weight loss. Once pregnant women with PCOS are at an increased risk of miscarriage, GDM, pregnancy-induced hypertension, and preeclampsia. [58] These complications are increased in hyperandrogenic phenotypes.

Behavioral / Emotional

PCOS is associated with a higher prevalence of psychiatric disorders. Both moderate to-severe depressive and anxiety symptoms are increased in cross-sectional studies [59], while a few longitudinal studies support an increased risk of incident depression and anxiety. [60] However, there is limited data on the persistence of depressive and anxiety symptoms in adolescents and beyond the fourth decade, although recent data implies psychological distress prevails long-term. [61, 62] In addition, women with PCOS have a higher prevalence of disordered eating [63] and body image distress. [64] Interestingly, in the latter study, various aspects of body image distress predicted anxiety and depressive scores, indicating that improvement in body image could potentially decrease anxiety and depressive symptoms. Both eating disorders and body image distress add to the difficulty in losing weight, highlighting the importance of routine screening for these disorders and the use of interventions such as cognitive behavioral therapy. [59, 65]

Quality of Life

PCOS symptoms and comorbidities burden women with PCOS. Women with PCOS report poorer health status than non-PCOS counterparts [66] and indeed, health professionals and women should be aware of the adverse impact of PCOS on health-related quality of life [67, 68], which seems to prevail at least until the late reproductive years [66].

What is remaining to be clarified

Cardiovascular disease

The risk of dyslipidemia, DM, and metabolic syndrome in older women with PCOS have been compared in fewer studies relative to the outcomes of obesity and impaired glucose tolerance. Most of the available data in perimenopause and beyond is obtained from small cross-sectional studies that included women with a presumed diagnosis of PCOS, limiting the validity of the findings. In order to adequately counsel patients, the prevalence of traditional CVD biomarkers needs to be assessed in different phenotypes of PCOS. There is some evidence for increased subclinical atherosclerosis in young women with PCOS. An increase in carotid intima-media thickness measurements has been described [69], with data suggesting an increased risk for stroke and myocardial infarction. [50] Ultimately, we need more longitudinal studies examining the incidence of cardiovascular events in this population. Although there is some evidence from population-based studies for increased cardiovascular events in late reproductive-age women with PCOS, most studies lack adequate power to evaluate these outcomes and do not include menopausal women with well-defined PCOS. [70]

Perimenopausal Disease Course

In a large proportion of women, the clinical features of PCOS improve with age, such that by the fourth decade the menstrual cycles become more regular and serum androgen levels normalize. [34] High serum levels of AMH and high antral follicle
counts suggest increased ovarian reserve in early reproductive years. These biomarkers also decrease with age, and their trajectory suggests that women with PCOS may go through menopause later than controls. [71]

X. Dietary Patterns In PCOS

There are certain diet plans to follow during PCOS that helps individual to recover, as described in the below diagram (Fig. 10.1).

**Mediterranean diet**

The Mediterranean diet (MedDiet) is recognized as the healthiest dietary model and has been included in international guidelines among recommended healthy dietary patterns because of its unique characteristics, including regular consumption of unsaturated fat, fiber, low-glycaemic index (low-GI) carbohydrates, antioxidants, and vitamins, as well as appropriate amounts of animal-derived protein. [72]

**Ketogenic Diet**

The ketogenic diet (KD), or keto diet, is a high-fat and low-carbohydrate diet that encourages forgoing nearly all carbohydrates, consuming high levels of fat (generally exceeding 70% of calories consumed), and avoiding excess protein, resulting in high production of ketones (principally acetoacetate and β-hydroxybutyrate) and nutritional ketosis. The KD is known for its antiepileptic effects in the treatment of refractory epilepsy. [73] KD has also been proposed as an effective treatment for other neurological disorders, including Alzheimer’s disease, Parkinson’s disease, and autism.

**Dietary Approaches to Stop Hypertension**

The Dietary Approaches to Stop Hypertension (DASH) dietary pattern, a low-GI and low-energy-dense diet, was primarily designed for lowering blood pressure and emphasizes fruits, vegetables, whole grains, nuts, legumes, and fat-free/low-fat dairy products while recommending low consumption of saturated fats, cholesterol, red and processed meats, refined grains, and sweets. This diet results in the consumption of higher amounts of dietary fiber, folic acid, phytoestrogens, potassium, magnesium, and other beneficial nutrients. [74, 75]

**Low-GI (Glycemic Index) Diets**

Low-GI diets are defined as those that obtain most carbohydrates from low-GI sources (Fig. 10.1). Foods having carbohydrates that are digested, absorbed, and metabolized slowly are regarded as low-GI foods. [76]

**Pulse-based Diet**

Pulses (e.g., lentils, chickpeas, split peas, and dry beans) are high in fiber and low in fat, contain high-quality protein and complex carbohydrates with a low GI, and are a significant source of vitamins and minerals, such as iron, zinc, folate, calcium, magnesium, and potassium. [77] Pulses, alone or as part of low-GI or high-fiber diets, improve markers of longer-term glycemic control in humans [78], and the pulse diet (Fig. 10.1) has been used in clinical populations to improve or maintain insulin sensitivity and prevent or reduce IR. [79] Pulse consumption has been shown to improve cardio metabolic disease risk factors in women with PCOS. [80] However, it is even more noteworthy that the phytochemicals, saponins, and tannins found in pulses have significant anticancer effects; in addition, adequate folate intake could reduce the risk of endometrial carcinoma, and the risk of endometrial carcinoma in women with PCOS is increased from 2 to 6-fold. [81] Thus, the possible positive effects of a pulse-based diet in women with PCOS are worth further study.

<table>
<thead>
<tr>
<th>Dietary</th>
<th>Key components</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MedDiet</strong></td>
<td>Extra-virgin olive oil</td>
<td>The main source of health-promoting component</td>
</tr>
<tr>
<td></td>
<td>Polyphenols</td>
<td>Slow the progression of the inflammatory status, &amp; improve both insulin sensitivity &amp; compensatory hyperinsulinemia</td>
</tr>
<tr>
<td></td>
<td>Vitamin E &amp; oleic acid</td>
<td>Treat chronic inflammation &amp; cancer</td>
</tr>
<tr>
<td></td>
<td>Resveratrol</td>
<td>Reduce androgen production</td>
</tr>
</tbody>
</table>
XI. Treatment Options In The Management Of PCOS

The conventional medical management of PCOS is symptomatic treatment and lifestyle modification with weight reduction. Usually, Metformin, oral contraceptives, anti-androgens, clomiphene citrate, and thiazolidinediones are used for the management of different presentations of PCOS. These drugs provide temporary, symptomatic relief and are not without side effects. So, here is a complete summary of treatment possible in various situations during PCOS, along with their adverse effects:

Table 1 Diet plans for PCOS

<table>
<thead>
<tr>
<th>KD</th>
<th>Nutritional ketosis</th>
<th>Decrease androgen secretion, increase SHBG, improve insulin sensitivity, &amp; renormalize endocrine functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whey or vegetable protein</td>
<td>Healthier gut microbiota</td>
<td></td>
</tr>
<tr>
<td>DASH</td>
<td>Antioxidants, folic acid, magnesium &amp; dietary fibre</td>
<td>Improve the abnormal metabolic profile &amp; IR.</td>
</tr>
<tr>
<td>Calcium &amp; folate</td>
<td>The potential favourable effects on IR &amp; inflammation</td>
<td></td>
</tr>
<tr>
<td>Low-GI</td>
<td>Low-GI foods (GI≤55 on the glucose scale)</td>
<td>Improve common clinical manifestations of PCOS</td>
</tr>
<tr>
<td>PBD</td>
<td>Phytochemicals, Saponins &amp; tannins</td>
<td>Significant anticancer effects</td>
</tr>
<tr>
<td>Adequate folate</td>
<td>Reduce the risk of endometrial carcinoma</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Treatment Approaches in PCOS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Place in therapy</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthetic Drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td>Hyperinsulinemia, Androgen excess,</td>
<td>Nausea &amp; Vomiting (common), Diarrhoea, Metallic taste, Lactic acidosis</td>
</tr>
<tr>
<td></td>
<td>Anovulation</td>
<td></td>
</tr>
<tr>
<td>Spironolactone</td>
<td>Hirsutism, acme</td>
<td>Irregular menstrual cycles, Hyperkalaemia, Hypotension</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>Regulation of menstrual cycle, Hirsutism, prevention of endometrial cancers</td>
<td>Weight gain, fluid retention, breast tenderness</td>
</tr>
<tr>
<td>Clomiphene Citrate</td>
<td>Ovulation induction</td>
<td>Mood swings, blurred vision, multiple gestations</td>
</tr>
<tr>
<td>Gonadotropins</td>
<td>Ovulation induction</td>
<td>Ovarian hyperstimulation, multiple pregnancies, abdominal pain, breast tenderness.</td>
</tr>
<tr>
<td>Pioglitazone, Rosiglitazone</td>
<td>Hyperinsulinemia, androgen excess, anovulation</td>
<td>Weight gain, edema, cardiovascular diseases</td>
</tr>
<tr>
<td>Myo-inositol &amp; d-chiro-inositol</td>
<td>Androgen excess, anovulation</td>
<td>Nausea, difficulty sleeping, headache, tiredness</td>
</tr>
<tr>
<td>Liraglutide, Exenatide</td>
<td>Weight loss, Anovulation, Hyperandrogenism, Hyperinsulinemia</td>
<td>Nausea, Abdominal discomfort</td>
</tr>
<tr>
<td>Sitagliptin, Alogliptin &amp; Linagliptin</td>
<td>Hyperinsulinemia, obesity</td>
<td>Headache, upper respiratory tract infections</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>Obesity, androgen excess, Hyperinsulinemia</td>
<td>Dizziness, headache</td>
</tr>
<tr>
<td>Statins</td>
<td>Hyperandrogenism, Dyslipidaemia</td>
<td>Worse IR</td>
</tr>
<tr>
<td>Bromocriptine</td>
<td>Anovulation</td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Hyperandrogenism, regulation of menstrual cycles.</td>
<td>Weight loss or poor appetite</td>
</tr>
<tr>
<td>Calcium</td>
<td>Regulation of menstrual cycles, anovulation</td>
<td>Dry mouth, headache</td>
</tr>
<tr>
<td>Eflomithine</td>
<td>Hirsutism</td>
<td>Acne, swollen patches, dry or tingling skin</td>
</tr>
<tr>
<td>Traditional Medicines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cinnamon</td>
<td>Hyperinsulinemia, regulation of menstrual cycles.</td>
<td>Nausea, hives, itchy eyes</td>
</tr>
<tr>
<td>Flax seeds</td>
<td>Hyperandrogenism, regulation of</td>
<td>Loose stools, delayed clotting time</td>
</tr>
</tbody>
</table>
Thus, various options are available for management, and after diagnosing it perfectly, people will have a better choice. [82]

XII. Yoga Practice

Conventional medicines are available as described above, but they provide temporary, symptomatic relief. They do not give a permanent cure for the disease. So, yoga can be the best solution to cure PCOS naturally and permanently. One study revealed that yoga interventions can manage polycystic ovarian patients. There was regularization of the menstrual cycle and restoration of ovulation and ovarian morphology after yoga therapy. A significance in the anthropometric measurements (body weight, BMI) was reported. A reduction of 5% in body weight can restore regular menstruation and improve response to ovulation. Some other studies also reported improvement in PCOS patients due to yoga therapy. The cause of improvement may be improved blood circulation to the pelvic viscera. Yoga mainly improves reproductive functions by reducing stress and balancing the neurohormonal profile. [83]

Here is a list of Yoga and its time duration to follow at least 5 days per week.

Table 3 Yoga chart with a duration of time, per day

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Yoga Practice</th>
<th>Duration (60 min) / per day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sitting series</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Titali asana (butterfly pose), Baddhakonasana, Chakkichalanasana, Ardhaushtrasana</td>
<td>10 mins</td>
</tr>
<tr>
<td></td>
<td>Supine series</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Utranapadasana, Sarvangasana, Halasana, Matsyasana, Shavasana</td>
<td>10 mins</td>
</tr>
<tr>
<td></td>
<td>Relaxation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Deep relaxation techniques</td>
<td>10 mins</td>
</tr>
<tr>
<td></td>
<td>Prone series</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bhujangasana, Shalabhasana, Makarasana</td>
<td>7 mins</td>
</tr>
<tr>
<td></td>
<td>Standing series</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tadasana, Trikonasana, Veerabhadrasana</td>
<td>7 mins</td>
</tr>
<tr>
<td></td>
<td>Pranayama</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dirghhaswash pranayama, Nadishuddhi pranayama, Kapalabhati pranayama, Ujjai pranayama, Bhramari</td>
<td>10 mins</td>
</tr>
<tr>
<td></td>
<td>Meditation (om kara naad)</td>
<td>6 mins</td>
</tr>
<tr>
<td></td>
<td>Kunjal kriya</td>
<td>Weekly once</td>
</tr>
</tbody>
</table>

XIII. Conclusion

Polycystic ovarian syndrome (PCOS) is a common endocrine system disorder in women of reproductive age. There are various risk factors that have been investigated in relation to PCOS, including obesity, genetic factors, glucose intolerance, and dyslipidemia. Insulin resistance is known to play a critical role in the pathophysiology of PCOS. Several studies suggest the use of new or modified therapies for the treatment of obesity and metabolic syndrome associated with PCOS. Recent clinical trials have focused on inositol, statins, Letrozole, and vitamin D for treating PCOS. On the other hand, studies on traditional/folk medicine in the treatment of PCOS are inconclusive and need to be fully investigated with reference to their efficacy and safety profiles. But, yoga is proven to be beneficial for a permanent solution, which needs consistent efforts. Overall continued and comprehensive research for new strategies in the treatment of PCOS is the need of the highest priority, as it can pave way for better therapeutic regimens for PCOS patients, improve their quality of life and prevent the development of comorbidities.

XIV. Acknowledgement

Firstly, I am grateful to The Almighty God, for establishing me to complete this successful review work. It is not possible to prepare a project report without the assistance and encouragement of other people. This one is certainly no exception. On the very outset of this report, I would like to express my sincere gratitude towards my guide Dr. Vipulkumar Gajera, Associate Professor at, Shree Naranjibhai Lalbhai Patel College of Pharmacy, Umra, who have helped me in this endeavour. Without his guidance, help, cooperation, encouragement and efforts, I would not have made headway in the project. I am also thankful to Dr. Ketan V. Shah, Professor & Principal at Shree Naranjibhai Lalbhai Patel College of Pharmacy, Umra, for undeniable motivation and providing an opportunity. Majorly, as I always blessed being a child of My Wonderful Parents, who helped me
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**Abbreviations**

- GLP-1: Glucagon-like peptide 1
- DDP-4: Dipeptidyl Peptidase-4
- LH: Luteinizing hormone
- FSH: Follicle-stimulating hormone
- SGLT2: Sodium-glucose Cotransporter-2
- DHEA-S: Dehydroepiandrosterone sulfate
- AMH: Anti-mullerian hormone
- HSD17B3: Hydroxysteroid 17-beta dehydrogenase 3
- BMI: Body mass index
- CVD: Cardiovascular disease
- DM: Diabetes Mellitus
- GDM: Gestational Diabetes Mellitus
- SHBG: Sex hormone binding globulin
- IR: Insulin Resistance

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