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## A Review on: Role of Nutritional in Polycystic Ovary Syndrome



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### ABSTRACT

Polycystic ovarian syndrome (PCOS) is an endocrine disorder associated with metabolic syndrome. This disorder can cause long-term insulin resistance, miscarriage, or even infertility in women. It is primarily characterised by elevated levels of male hormones (androgens), acne, and hirsutism. The most common cause of infertility, polycystic ovary syndrome (PCOS) is affects reproductive aged women with a prevalence ranging from 4% to 18%. Patients with PCOS can exhibit a wide range of signs and symptoms, making it challenging to grade the condition precisely. The WHO estimates that there are more than 116 million (3.4%) women worldwide who have PCOS. Depending on the method of diagnosis, 8.2% to 22.5% of women in India are thought to be affected. The risk factors for PCOS include irregular periods, a history of diabetes and infertility in the family, the mother's irregular periods, bad moods, and a lack of exercise. The primary pathophysiological characteristics of PCOS are hormonal imbalance, insulin resistance, and hyperandrogenism that damage folliculogenesis and increase the risk of associated conditions like endometrial cancer and type II diabetes. Natural and allopathic remedies that work to interfere with the PCOS mechanism can be used to treat PCOS. In addition to offering some evidence-based dietary recommendations for use in clinical practise, the goal of this review was to describe and assess the effects of dietary interventions on outcomes related to PCOS.



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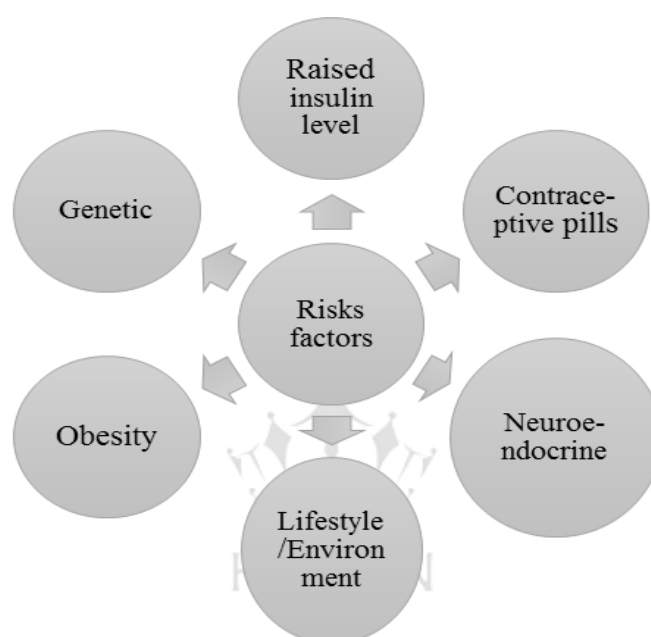
## INTRODUCTION:

Polycystic ovarian syndrome (PCOS) is an endocrine disorder associated with metabolic syndrome. It is characterized by manifestations of anovulation, ovarian cyst and endocrine variables that affect a woman's health and life. The most common cause of infertility, polycystic ovary syndrome (PCOS) affects reproductive-aged women with a prevalence ranging from 4% to 18%. It is linked to reproductive, metabolic, and hormonal dysfunction as well as a higher association with pregnancy complications<sup>[1,2]</sup>. PCOS is an autoimmune, polygenic, systemic, inflammatory, dysregulated steroid state, and inflammatory disease that primarily manifests as a result of poor lifestyle choices<sup>[15]</sup>. Stein and Leventhal were the first to identify PCOS as a syndrome of polycystic ovarian disease and oligo-amenorrhea, which was occasionally accompanied by hirsutism, acne, and obesity<sup>[3]</sup>. In general, women with PCOS weigh more than women without PCOS, and numerous studies have found that more than half of obese women with PCOS also tend to gain weight more quickly than women without PCOS over time<sup>[2]</sup>. A clinical sign of PCOS, hyperandrogenism prevents the development of follicles, the formation of ovarian microcysts, and menopause<sup>[1]</sup>. Patients with PCOS can exhibit a wide range of signs and symptoms, making it challenging to grade the condition precisely. The criteria of the ESRHE/ASRM Rotterdam consensus meeting, which expanded the prior NIH classification of 1990, are currently used to diagnose PCOS. It was founded on at least two of the qualities listed below: using ultrasound to detect oligo-anovulation, hyperandrogenism, and polycystic ovaries<sup>[4]</sup>. About 6–10% of older women typically have this complex disease. The WHO estimates that there are more than 116 million (3.4%) women worldwide who have PCOS. Depending on the method of diagnosis, 8.2% to 22.5% of women in India are thought to be affected<sup>[1]</sup>. LSM (lifestyle modification; diet, exercise, and cognitive behaviour therapy) and pharmacotherapy, including clomiphene citrate (CC), aromatase inhibitors, low-dose human menopausal gonadotropin (hMG) or FSH, insulin sensitizers, laparoscopic ovarian drilling, and in vitro fertilisation, are common treatment modalities used in women with PCOS (IVF)<sup>[2]</sup>.

## Causes and Risk Factors:

The risk factors for PCOS include irregular periods, a history of diabetes and infertility in the family, the mother's irregular periods, bad moods, and a lack of exercise. The majority of PCOS patients start having irregular periods in their teens, and endocrine dyscrasia in any area of the hypothalamic-pituitary-gonadal axis can cause both irregular periods and

anovulation 191. A significant high risk factor for PCOS is a family history of diabetes, particularly if it is an inherited metabolic disorder. The daughter's increased risk of developing PCOS is also correlated with her mother's irregular menstrual cycles [5]. Obesity, hypertension, hyperlipidemia, glucose intolerance, and hyperinsulinemia have all long been recognised as risk factors for cardiovascular disease. Recent studies have demonstrated that elevated plasma levels of the anti-inflammatory proteins C-reactive protein (CRP) and homocysteine (Hcy) pose a significant long-term risk for atherosclerosis and chronic vascular damage.



**Fig. 1: Risk factors of PCOD [7,8]**

**Obesity:** Weight gain and obesity are frequently the cause of PCOS's clinical and biochemical manifestation in women who are genetically predisposed to the condition. As a result, obesity and PCOS are closely related. 38% to 88 percent of women with PCOS are overweight or obese [9]. When compared to either their nonobese PCOS counterparts or obese women without PCOS, obese women with PCOS may have additive risks for associated comorbidities, despite the fact that the syndrome is now known to occur in both lean and obese women [10]. Adolescent obesity is widespread throughout the world. Women's obesity and the polycystic ovary syndrome (PCOS), which has serious metabolic and reproductive health implications, are frequently linked. Despite the fact that PCOS doesn't show clinical signs until early adolescence, its causes are probably much older [11].

**Lifestyle/ Environment:** A reversible metabolic disorder called polycystic ovary syndrome significantly contributes to the global epidemic of chronic diseases linked to poor lifestyle choices. The role of various lifestyle factors in the pathogenesis of PCOS has been researched. Diet, exercise, stress, sleep disturbance, circadian disruption, and exposure to chemicals in the environment are a few of these. Recent developments in the fields of evolutionary biology, computer technology, artificial intelligence, genomics, epigenetics, metabolomics, and nutrigenomics are shedding light on the mechanisms by which lifestyle factors affect the pathogenesis of PCOS [12].

**Neuroendocrine:** An important pathophysiologic aspect of PCOS is reproductive neuroendocrine dysfunction, which is characterised by increased frequency and amplitude of gonadotropin-releasing hormone (GnRH) release, as indicated by pulsatile luteinizing hormone (LH) secretion [13]. When estradiol is present, which activates hypothalamic progesterone receptors, the normal luteal slowing of GnRH and LH pulse frequency occurs through feedback inhibition by elevated progesterone levels [14].

**Contraceptive Pills:** By inhibiting ovulation and preventing cyst formation, the oral contraceptive pill (OCP) can reduce hyperandrogenism and regularise menstrual cycles. Venous thrombosis is a danger, though. Additionally, it lowers serum 25-hydroxyvitamin D levels, which may have an impact on bone health. The plasma levels of ICAM-1, MCP-1, and TNF- are raised in PCOS patients receiving this treatment. Despite being inflammatory, these cytokines normalise the metabolic parameters, such as plasma glucose, lipids, and insulin [15].

**Raised Insulin level:** Depending on the level of obesity, 10% to 25% of the general population suffer from insulin resistance (IR). In contrast, 4% to 6% of women of reproductive age experience polycystic ovary syndrome (PCOS), which appears to be unaffected by race or ethnicity and affects many of these women in addition to IR [16]. Additionally, type 2 diabetes mellitus, hypertension, dyslipidemia, and cardiovascular disease are all more common in affected women. Future studies are likely to emphasise the role of insulin resistance in the syndrome because it is present in 50–70% of women with PCOS and is now widely acknowledged as a significant risk factor for the development of the metabolic syndrome in such women [17].

**Genetic:** Both PCOS and obesity are diseases whose development is influenced by genetic factors. There is evidence for shared genetic architecture between metabolic traits, including a causal relationship between obesity and PCOS, according to a recent large-scale genome-

wide meta-analysis of PCOS. Given the epidemiological connection between the two diseases, it is crucial to take genetic variants potential roles into account <sup>[9]</sup>.

### **Complication:**

A complex disorder called PCOS can have an effect on numerous organ systems. PCOS can cause serious long-term complications like endometrial cancer, heart disease, diabetes, and metabolic syndrome if it is not properly managed. Gestational diabetes and gestational hypertensive disorders can develop during pregnancy. Age-related metabolic diseases like dyslipidemia, type 2 diabetes, and glucose intolerance are frequently mentioned. Women with PCOS have higher baseline cardiovascular risks and more subclinical vascular disease, but there is no evidence that these factors are associated with higher cardiovascular morbidity and mortality. And lastly, women with PCOS appear to have a higher incidence of endometrial cancer<sup>[18]</sup>.

**Cardiovascular disease:** Cardiovascular disease in PCOS-affected women was the subject of numerous observational studies. They still come to contradictory conclusions. Based on a poor cardiovascular profile and surrogate markers for cardiovascular disease like flow-mediated dilation, carotid intima-media thickness, and coronary artery calcium, women with PCOS are more likely to develop cardiovascular disease <sup>[18,19]</sup>. There is no clear evidence that women with PCOS have a higher cardiovascular morbidity or mortality rate. However, a personal history of clinical hyperandrogenism or menstrual disorders in post-menopausal women puts them at higher risk for cardiovascular disease. The definition of PCOS, cardiovascular endpoints, and patient median age varied between studies. It can be challenging to diagnose PCOS retroactively after menopause because some series were very small, some patients were too young to have time to develop cardiovascular disease, and so on<sup>[18]</sup>.

**Endometrial cancer:** Endometrial cancer (EC) is a serious risk for women with polycystic ovarian syndrome (PCOS). Due to the disease burden of EC and its monetary costs, finding a safe and effective method to prevent EC in women with PCOS is crucial. EC incidence appears to be increasing globally, particularly as obesity rates rise <sup>[20]</sup>. The over-secretion of luteinizing hormone (LH) is one of the hormonal traits of PCOS. LH receptors are reported to be highly expressed in PCOS women's endometrium with endometrial hyperplasia and carcinoma. In this way, LH encourages the development of cultured human endometrial cells <sup>[21]</sup>.

**Diabetes:** In comparison to the general population or a control population that was matched for age and race, cross-sectional and prospective population-based studies have repeatedly demonstrated that PCOS is linked to a higher chance of developing Type 2 diabetes or impaired glucose tolerance (IGT)<sup>[22]</sup>. A family history of diabetes significantly increases the risk of developing diabetes, according to numerous studies. The likelihood of developing type 2 diabetes is correlated with the number and closeness of relatives who have the disease. When compared to PCOS women without a family history, it has been discovered that insulin secretory defects in PCOS women with a family history of diabetes are more severe<sup>[23]</sup>.

**Metabolic syndrome:** The MS is a group of connected risk factors for diabetes and cardiovascular disease<sup>[24]</sup>. The geographical region as well as the patients' habits appear to have an impact on the prevalence of MS in PCOS patients. The condition known as MetS, also called Syndrome X, is a conglomeration of several diseases, including central abdominal obesity, hypertension, dyslipidemia, and hyperglycemia, all of which are major risk factors for cardiovascular diseases. These abnormalities, which are primarily caused by complex multi-organ interactions of IR, obesity, and age, are present in MetS patients to varying degrees<sup>[25]</sup>. Women with PCOS have a twice as high risk of developing MS as women without PCOS who are the same age and BMI. In addition, younger women with PCOS have a higher risk of developing MS than women in the general population. Additionally, along with other biochemical cardiovascular risk factors, obese and thin women with PCOS frequently exhibit an atherogenic lipid profile<sup>[24]</sup>.

### **Pathophysiology:**

PCOS is primarily characterised by hyperandrogenism, infertility, lack of ovulation, increased level of LH, increased insulin resistance, decreased sex hormone-binding globulin (SHBG), and hirsutism, which can be seen and diagnosed by ultrasound and laboratory tests<sup>[26]</sup>. PCOS manifests as a phenotype that reflects a vicious cycle that includes ovarian, neuroendocrine, and metabolic dysfunction. Numerous theories have been put forth over the years regarding the proximate physiologic causes of PCOS. PCOS is a result of interactions between numerous proteins and genes that are influenced by environmental and epigenetic factors<sup>[27]</sup>. Serum concentrations of androgens like testosterone, androstenedione, and dehydroepiandrosterone are probably high in women with PCOS due to disruptions in the secretion rate and metabolism of androgens and oestrogens in these women<sup>[28,29]</sup>. AMH production per granulosa cell is increased on average 75-fold in granulosa cells of

anovulatory PCOS compared to granulosa cells of normal ovaries, according to research that found the concentration of AMH in ovarian fluid from anovulatory PCOS women to be 5-fold higher than that of ovulatory women<sup>[30]</sup>. Furthermore, it is highly likely that some complications, such as hyperinsulinemia and environmental insulin resistance, will occur. Obesity is a result of these complications in varying degrees. Impaired insulin receptor signalling can lead to insulin resistance. As a result, the cell's ability to use insulin is compromised, which leads to an additional rise in insulin secretion to make up for its deficiency. Due to insulin resistance, patients with PCOS experience a decrease in adiponectin with an increase in the effect of gonadotropins on ovarian function <sup>[29]</sup>.

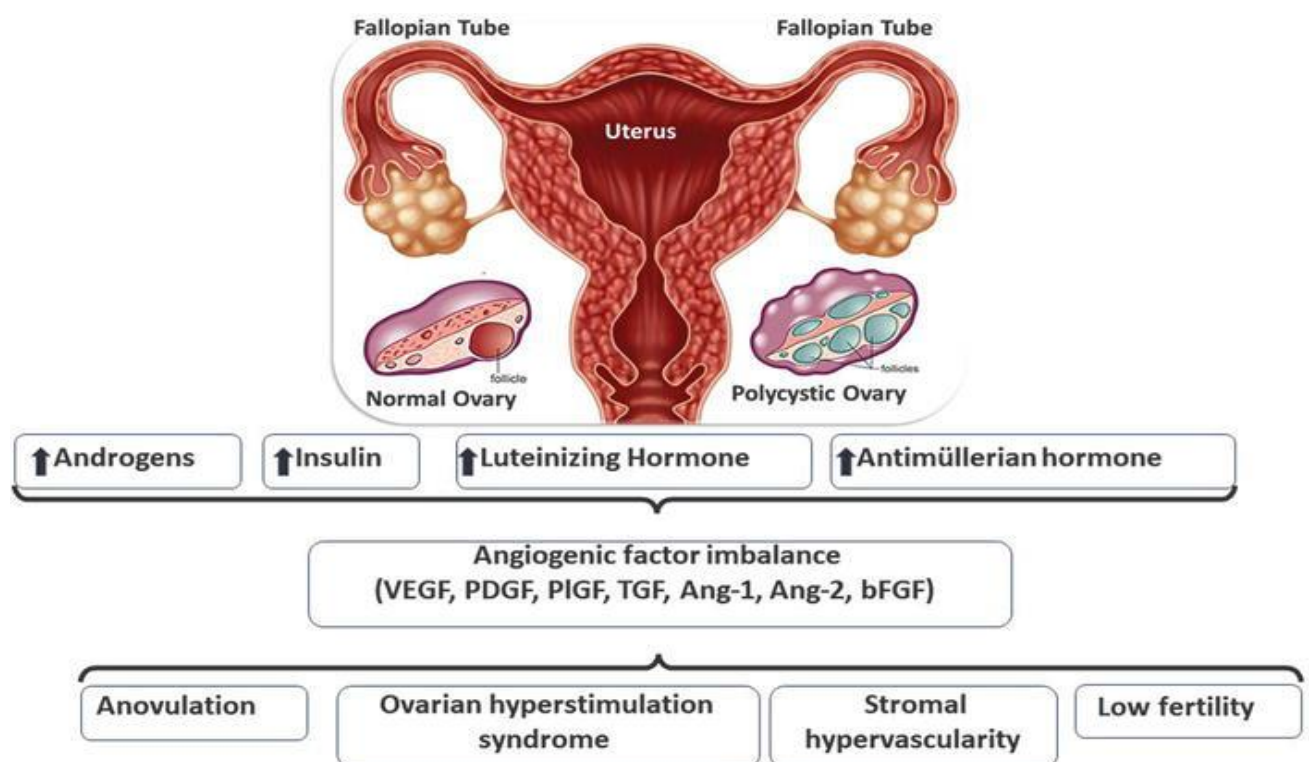


Fig. 2: Pathophysiology of polycystic syndrome <sup>[31]</sup>

### Management of PCOS:

The polycystic ovary syndrome condition is now incurable. Only managing the PCOS symptoms is the sole goal of the clinically used treatment <sup>[32]</sup>. The hormonal imbalance associated with PCOS cannot be corrected; changes in lifestyle are primarily responsible for improvements in symptoms. At the moment, efforts are focused on anovulation, infertility, or the treatment of PCOS-related symptoms.

Currently, PCOS management options include

Allopathic remedies

Nutritional Management

### **Allopathic remedies:**

#### **Metformin:**

It is used to treat insulin resistance and restore irregular menstruation in PCOS used to treat insulin resistance and restore irregular menstruation in PCOS .Metformin improves insulin resistance in PCOS patients by increasing glucose absorption and utilisation <sup>[8]</sup>. It balances glucose levels, as opposed to other insulin-regulating medications that have the side effect of either hypo- or hyperglycemia<sup>[33]</sup>. Metformin acts indirectly by lowering insulin levels and decreasing the activity of the CYP17 cytochrome, which is involved in the production of androgens. It also raises SHBG levels, which further reduces free testosterone <sup>[34]</sup>. The long-term issues connected to PCOS in women, such as endometrial cancer, type 2 diabetes, cardiovascular disorders, and hypertension, can be controlled with metformin <sup>[8]</sup>.

#### **Thiazolidinediones:**

The oral antidiabetic drug class identified as thiazolidinediones. A variety of insulin-resistant conditions, such as obesity, impaired glucose tolerance (IGT), and polycystic ovarian syndrome, have been demonstrated to benefit from the use of TZDs, which have been shown to increase insulin sensitivity (PCOS) <sup>[35]</sup> (TZDs) is new. Thiazolidinediones lower insulin resistance by enhancing muscle and adipose tissue's sensitivity to insulin and by preventing hepatic gluconeogenesis. The most extensively researched thiazolidinedione for treating PCOS is troglitazone, the first medicine in this family to become commercially accessible<sup>[36]</sup>.

#### **Clomiphene citrate:**

While not always being successful in superovulation prevention or ovulation induction, clomiphene citrate is still the first line of treatment for PCOS patients <sup>[37]</sup>.The main medication for triggering or enhancing ovulation is currently clomiphene citrate (CC). Yet not all circumstances lend itself to its success. 15% to 20% of patients experience clomiphene resistance, which is defined as the continuation of anovulatory symptoms despite receiving normal CC treatment. The cervical mucous and endometrium may also be negatively impacted by CC <sup>[38]</sup>.



**Letrozole:**

Letrozole, an aromatase inhibitor, has demonstrated efficacy in treating PCOS patients. Letrozole, a more recent ovulation-inducing drug, was first used to treat breast cancer. Letrozole, an aromatase inhibitor, is thought to trigger ovulation by momentarily reducing E levels and triggering a reflexive rise in FSH. Letrozole does not appear to directly affect the endometrium because it does not bind the ER. Only letrozole caused a proportional increase in the endometrium's LIF protein expression, even though letrozole also boosted LIF's mRNA expression [37].

**Nutritional Management:**

A significant factor in PCOS is nutritional supplementation. Simple nutritional supplements may lessen these risks by reversing PCOS's response to oxidative stress. Supplements of vitamins, minerals, probiotics, and other dietary additives can be very helpful in easing PCOS related symptoms [63].

Sr. no.	Nutrition	Activity
1.	Vitamin	Vitamins are a diverse selection of organic substances that are necessary for healthy body function. The amount of vitamins in food has also increased to keep up with their bioavailability, metabolism, and health-promoting activities [85].
	Vitamin A	In overweight women with PCOS, higher retinol-binding protein 4 (RBP4) levels are linked to obesity and impaired glucose metabolism. RBP4 expression was measured in isolated subcutaneous and omental adipose tissue from women with PCOS, according to a different RBP4-based investigation [39].
	Vitamin D	Endometrial proliferation is reduced by vitamin D, lowering the likelihood of developing endometrial cancer. Moreover, by altering the endometrium, it can enhance the success of embryo implantation and pregnancy. In light of these research, it can be concluded that vitamin D supplements may be effective in preventing pcos-related illnesses [40].
	Vitamin B	This group includes vitamins B6, B12, and folic acid due to the

		growing significance of homocysteine (Hcy) in PCOS. According to this mechanism, high levels of total plasma Hcy, an essential amino acid obtained from dietary methionine, enhance the risk of PCOS's reproductive and cardiovascular symptoms <sup>[41]</sup> .
	Vitamin E	Women with PCOS who received 400 IU of vitamin E and 1,000 mg of omega-3 fatty acids daily for 12 weeks saw a significant improvement in the IR and androgen levels <sup>[39]</sup> .
2.	Mineral	The metabolic profile, mental health, ovulation, and menstrual cyclicity are just a few of the areas that dietary supplements are expected to benefit. Current research on PCOS has focused on mineral supplementation as a means of treating its pathologic conditions <sup>[41]</sup> .
	Zinc	There has been some research of zinc's significance in endocrine disorders like PCOS. Zinc supplementation has been shown in several trials to have positive effects on PCOS's metabolic and endocrine symptoms. The antioxidant properties of zinc are responsible for these metabolic benefits brought on by supplementation <sup>[42]</sup> .
	Selenium	Selenium is a fundamental part of selenoproteins, which are extremely important for maintaining human health. Se have an impact on insulin resistance, making it possible to assess how they change in relation to PCOS <sup>[43]</sup> .
	Magnesium	Magnesium (Mg) is a necessary nutrient for both energy production and nucleic acid synthesis. Almost 300 enzyme systems use it as a cofactor. Women with PCOS are more prone to under eat foods high in magnesium and have lower serum magnesium values <sup>[44]</sup> .
	Chromium	Chromium is a trace element that has not yet been extensively researched as a treatment for PCOS. It has been demonstrated that chromium lowers triglyceride levels in people. Because it increases insulin sensitivity, chromium may help adult individuals with PCOS symptoms <sup>[45]</sup> .
	Calcium	Many studies have shown the importance of calcium in the pathophysiology of PCOS, the development of follicles, and

		ovulation. It is thought that their function in this area is unaffected by insulin resistance. Likewise, it appears that they play a significant role in the transformation of testosterone into oestrogens in granulosa cells, which ultimately created a balanced level of androgen and oestrogen in PCOS patients [46].
3.	Carbohydrate	Excessive carbohydrate intakes especially refined carbohydrate intakes will make the body release more insulin to keep glucose levels in check. An insulin-resistant lady with PCOS may not be the ideal candidate for the standard low-fat, high-carbohydrate diet [47].
4.	Dietary	Diets that lower obesity and IR rates are advantageous for PCOS-afflicted women. The best diet for PCOS patients has not yet been identified, but dietary therapies as a first-line treatment have been studied. The prevention of this illness is greatly aided by a healthy diet and the maintenance of an adequate nutritional status, and the recovery of PCOS patients is much aided by therapeutics and dietary practises [48].
5.	Omega-3 Fatty acid	The regulation of aberrant gene expression in the pathogenesis of PCOS is linked to omega-3. In granulosa cell culture, the effects of omega-3 EPA at dosages ranging from 25 to 100 g were seen as increased insulin growth factor (IGF)-1 expression and decreased cyclooxygenase 2 (COX2) expression. IGF-1 is a crucial substance for follicular differentiation, and COX-2 helps to mature oocytes [49].
6.	Probiotic	In women with PCOS, probiotics may improve metabolism, lower serum testosterone, and reduce systemic inflammation when taken for 12 weeks [61].
7.	Bioflavonoids	Polyphenolic compounds, which are present in plants, make up bioflavonoids [84].

## Vitamin:

**Vitamin A:**The name "retinol" belongs to vitamin A, a fat-soluble vitamin. The antioxidant activity, steroid metabolism, oocyte nuclear maturation, and suppression of cumulus cell death are all influenced by vitamin A-derived metabolites like retinoids, retinoic acid, and retinol [50,51]. In overweight PCOS women, higher levels of retinol-binding protein 4 (RBP4) are linked to obesity and impaired glucose metabolism [41]. In theca interna cell cultures taken from PCOS and healthy women, the effects of retinol and retinoids, derivatives of retinol, were applied. Theca interna cells treated with trans retinol produced more dehydroepiandrosterone and mRNA for the enzyme cytochrome P450 17 hydroxylase (CYP17), which is implicated in androgen synthesis and retinol biosynthesis [52].

**Vitamin D:**A steroid hormone, vitamin D is largely produced by sunlight, with small amounts also coming from food sources including oily fish and fortified dairy. In addition to its vital role in calcium metabolism and bone homeostasis, vitamin D is thought to have significant metabolic and endocrine effects [53]. Women with PCOS are more likely to be vitamin D deficient than other women: 67 to 85% of PCOS patients have low vitamin D levels. Up to half of all adults may suffer from vitamin D insufficiency, which is a prevalent health issue [54]. Vitamin D receptors are found in the ovary, placenta, and endometrium. Vitamin D has been proven to improve cardiac dysfunction in PCOS murine models and restore endometrial function in PCOS patients [55]. In addition to its physiological role in reproduction, vitamin D also has an impact on ovarian follicular growth and luteinization, anti-müllerian hormone (AMH) signalling, follicle-stimulating hormone sensitivity, progesterone production in human granulosa cells, and follicle-stimulating hormone sensitivity. Moreover, it influences glucose homeostasis in a variety of ways [56].

**Vitamin B:**Homocysteine (Hcy) blood levels in women with polycystic ovary syndrome (PCOS) on short-term metformin treatment: effects of B-group vitamins and folic acid administration [57]. The serum levels of folic acid and vitamin B12 fall with metformin medication because metformin inhibits the binding of the intrinsic factor-B12 complex and its receptor. Hcy levels are raised by metformin. The levels of androgen and lipids in the pathophysiology of PCOS were unaffected by vitamin supplements [39]. Two studies have shed light on the relationship between metformin and B group vitamins. The first revealed that daily folic acid or B group vitamin administration could be useful in lowering increased Hcy levels in women with PCOS receiving short-term metformin therapy. The investigators

did note, however, that vitamin supplementation had no impact on androgen and lipid levels in the pathogenesis of PCOS [57]. In the second study, it was discovered that vascular endothelium benefited from metformin use combined with folate supplementation for six months. Since this therapy lowers Hcy levels, it can be useful in managing PCOS's long-term side effects, including as cardiovascular diseases [58].

**Vitamin E:** The antioxidant properties of vitamin E (also known as -tocopherol), an exogenous lipid-soluble substance, are widely known in the treatment of cancer, high-risk pregnancies, and infertility. By protecting the cell membrane from lipid peroxidation and activating intracellular antioxidant enzymes, vitamin E is assumed to be a direct free radical scavenger [59]. Body weight, Ang-1, Ang-1/Ang-2 ratio, and VEGF level all improved after 8 weeks of vitamin E treatment in PCOS women [60].

### **Minerals:**

The contribution of macro- and micronutrients to the development of this disease is essentially unknown. The composition of macro- and microelements in PCOS-afflicted women has only been the subject of individual studies. The fundamental micronutrients that are necessary for oxidative stress pathways and the metabolic processes of cells include copper, zinc, and manganese, as well as a large number of proteins and metalloenzymes [63].

**Zinc:** Zinc supplementation has been shown in several trials to have positive effects on PCOS's metabolic and endocrine symptoms. The antioxidant properties of zinc are responsible for these metabolic benefits brought on by supplementation [42]. A randomised, double-blind, placebo-controlled trial examined the effects of zinc supplementation on markers of insulin resistance and lipid profiles in women with polycystic ovary syndrome [64]. The metabolic and endocrine symptoms of PCOS have been positively impacted by zinc supplementation, according to several studies. Zinc's antioxidant properties can be used to explain the metabolic improvements brought on by supplementation with zinc [70]. Compared to placebo, taking zinc supplements for 8 weeks significantly reduced hirsutism and alopecia in PCOS women, but had no effect on hormonal profiles or acne. There is limited evidence that zinc supplementation improves female fertility and hormonal profiles [65].

**Selenium:** Selenium (Se) is essential for the development of reproductive tissue and is protective against oxidative stress. Women with PCOS have been linked to high androgen levels, free radicals, and low selenium levels [62]. In addition, supplementing PCOS women

with 200 microgram of Se plus  $8 \times 10^9$  colony forming units (CFU)/day for 12 weeks reduced body weight and adverse cardio-metabolic effects [66]. Se affects insulin levels, resulting in decreased body weight, BMI, IGF (insulin-like growth factors), and their binding proteins. Women with PCOS had higher levels of HOMA-IR and higher levels of insulin, according to a study by Coskun et al., but these differences were not statistically significant when compared to the controls [62,67].

**Magnesium:** Magnesium is an abundantly present essential macromineral in the human body that plays key roles in more than 300 biochemical processes, including those that control blood pressure, DNA and RNA synthesis, blood sugar levels, and the metabolism of carbohydrates, fats, and proteins. It is the most significant cation inside cells [68]. Numerous biochemical abnormalities linked to the gynaecological pathologies of PCOS can be brought on by magnesium deficiency. Women with PCOS are more prone to under eat foods high in magnesium and have lower serum magnesium values [44,69]. Due to its ability to reduce androgens and improve glucose homeostasis, as well as its anti-inflammatory and antioxidant properties, magnesium may help with the clinical symptoms of PCOS [70]. Magnesium co-supplementation for 12 weeks among PCOS women had positive effects on serum hs-CRP, plasma PCO, TAC, and gene expression of IL-1 and TNF-, compared to the placebo [71].

**Chromium:** Chromium is a trace element that has not yet been extensively researched as a treatment for PCOS [45]. It is essential for glucose and insulin homeostasis, as well as for the metabolism of carbohydrates, proteins, and lipids [72]. Foods and dietary supplements both contain trivalent chromium, also known as chromium 3. The Food and Nutrition Board of the Institute of Medicine estimates that US adults consume between 23 and 29 g and 39 to 54 g of chromium per day, respectively, from food. Trivalent chromium is found in chromium picolinate (CrP), which has undergone extensive research as a chromium dietary supplement [73]. Due to chromium's prior ability to increase insulin sensitivity, which has been demonstrated in some studies, it has been hypothesised that this substance may help adult patients with PCOS feel better [74].

**Calcium:** Many studies have shown the importance of calcium in the pathophysiology of PCOS, the development of follicles, and ovulation. It is thought that their function in this area is unaffected by insulin resistance [46]. Mammalian oocyte maturation depends heavily on calcium [75]. It is thought that their function in this area is unaffected by insulin resistance. Likewise, it appears that they play a significant role in the transformation of testosterone into

oestrogens in granulosa cells, which ultimately created a balanced level of androgen and oestrogen in PCOS patients [46].

### **Carbohydrate:**

A typical definition of a "low-carbohydrate diet" is one with 20–60 grammes of carbohydrates per day, or less than 20% of total calories. 84 Only one nonrandomized 24-week trial with a small sample size, which included PCOS subjects who were told to keep their daily carbohydrate intake to under 20 grammes, was one of 12 studies that examined the effects of low-carbohydrate diets<sup>[76]</sup>. For the metabolism of glucose and IR, carbohydrate distribution may be a key factor. According to one study, people with type 2 diabetes who consume the majority of their carbohydrates (50%) at lunch experience the lowest postprandial glucose spikes and have better glycemic control than those who consume their carbohydrates equally throughout the day or at breakfast, dinner, and lunch<sup>[77]</sup>.

### **Diets:**

The best diet for PCOS patients has not yet been identified, but dietary interventions as a first-line treatment have been evaluated. The prevention of this disorder is greatly aided by a healthy diet and the maintenance of an adequate nutritional status, and the recovery of PCOS patients is greatly aided by therapeutics and dietary practices<sup>[48]</sup>. Dietary management of PCOS has centered on weight loss in overweight women, with research demonstrating that weight loss of even 5% can lower insulin levels, enhance menstrual function, and lower serum testosterone. Dietary management should also put a strong emphasis on lowering the risk of diabetes and cardiovascular disease because these conditions are more common in women with PCOS, as are obesity, insulin resistance, and the subsequent hyperinsulinemia they cause<sup>[78]</sup>. For those with PCOS, dietary changes are the first line of treatment; however, it is unknown how frequently clinicians advise this course of action, and there is currently no accepted diet that is best for these women<sup>[79]</sup>. Four studies found no significant effects of dietary protein on markers of energy metabolism or androgenic parameters in women with PCOS. Two studies reported greater weight loss with higher protein intake, and three reported greater decreases in body fat with higher protein diets. For PCOS-afflicted women, consuming 7–15 g of dietary protein with meals and snacks may improve insulin sensitivity and reduce postprandial glucose fluctuations, but more research is needed to confirm this. Women with PCOS should be encouraged to adopt healthy eating habits like DASH or the Mediterranean-style diets because they are high in dietary fibre, antioxidants, and anti-

inflammatory nutrients, increase satiety, and have anti-hyperlipidemic, anti-hypertensive, and antidiabetic properties [76].

### **Omega-3 Fatty acid:**

The polyunsaturated fatty acids known as omega 3 fatty acids (PUFAs). The most well-known members of this group are eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and -linolenic acid. Each fatty acid has unique metabolic and endocrine characteristics, and consumption of PUFAs has been linked to decreased TG while consumption of MUFAs has been linked to decreased testosterone levels<sup>[80]</sup>. Omega-3 fatty acids have recently been investigated as potential therapeutics for the management of PCOS. It has been suggested that the regulation of abnormal gene expression in the pathophysiology of PCOS is connected to the healing mechanism of omega-3 fatty acids. For instance, different doses (ranging from 25 to 100 g) of omega-3 EPA increased the expression of IGF-1 and decreased the expression of COX2 in granulosa cell culture. It is evident that IGF-1 is a necessary substance for follicular differentiation and that COX-2 aids in the maturation of oocytes<sup>[81]</sup>. The regulation of abnormal gene expression in the pathophysiology of PCOS is linked to omega-3. In granulosa cell culture, the effects of omega-3 EPA at doses ranging from 25 to 100 g were seen as increased insulin growth factor (IGF)-1 expression and decreased cyclooxygenase 2 (COX2) expression. IGF-1 is a crucial substance for follicular differentiation, and COX-2 helps to mature oocytes<sup>[39]</sup>.

### **Probiotic:**

Dairy products contain probiotics, which are living microbial dietary supplements that work in harmony with the gut microbiota. Probiotics are helpful for metabolism, especially in inflammatory situations<sup>[41]</sup>. Women with PCOS have a less diverse gut microbiome than women without the condition, and there is evidence that their intestines are more permeable. Increased levels of systemic inflammation as well as hyperandrogenism have been connected to this decrease in gut microbial diversity<sup>[82]</sup>. The effects of multispecies probiotics used for 8 weeks as a probiotic supplement on pancreatic cells and C-reactive protein (CRP) in PCOS patients. Their study's findings indicated decreased fasting blood sugar and serum insulin levels in a rough model. Interestingly, there was little change in CRP levels<sup>[83]</sup>.



## Bioflavonoids:

Polyphenolic compounds, which are present in plants, make up bioflavonoids. Antioxidant, anti-diabetic, anti-estrogenic, anti-inflammatory, and antiproliferative properties are all possessed by flavonoids<sup>[84]</sup>. It contains anthocyanins, flavan-3-ols, flavanones, flavones, flavanols, and isoflavones, the latter of which is of particular interest given that it has been suggested that it promotes neuroplasticity and cardioprotection. The general anti-oxidant, anti-diabetic, anti-estrogenic, anti-inflammatory, and antiproliferative properties of bioflavonoids are well known, and some of their metabolites have been shown to demonstrate PCOS pathogenesis at various levels<sup>[82]</sup>. The intakes of the six flavonoid classes mentioned above in women with PCOS and metabolic syndrome were examined, and it was discovered that only flavanol consumption differed between groups (lower in metabolic syndrome) and was negatively correlated with metabolic syndrome<sup>[41,82]</sup>.

## CONCLUSION:

According to this review of the literature, nutritional supplementation with vitamins, minerals, vitamin-like nutrients, and complementary therapies may help to improve some of the adverse health consequences related to PCOS. Insulin resistance and obesity make PCOS a complicated issue. The use of medication as well as dietary and exercise modifications should therefore be part of treatments. PCOS management is crucial because it affects conditions like hirsutism, infertility, and irregular menstruation. Nutritional factors like high-fiber diets, balanced diets, low-calorie diets, and probiotics have a big impact on controlling PCOS.

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