International Journal of Current Innovations in Advanced Research
(International Multidisciplinary Tri-annual Research Journal)
Content Available at www.ijciar.com ISSN (O) 2636-6282 ISSN (P) 2659-1553

LIFESTYLE CHANGES AND NUTRITION IN POLYCYSTIC OVARIAN DISORDER: A HOLISTIC REVIEW

Archita Tiwari[1], Arti Verma[2], Shrishti Mishra[3], Bharat Mishra[4]*
[1] Khwaja Moinuddin Chishti language university, Lucknow
[2,3] Department of Pharmaceutics,RGS College of Pharmacy, Itaunja, Lucknow
[4] Institute of Pharmacy, Dr. Shakuntala Misra National Rehabilitation University, Lucknow

***Corresponding Author**
Prof. Dr. Bharat Mishra
Director, Institute of Pharmacy
Dr. Shakuntala Mishra National Rehabilitation University, Lucknow

DOI: https://doi.org/10.47957/ijciar.v7i2.170

Received: 05 Apr 2024 Revised: 22 Apr 2024 Accepted: 16 May 2024

Abstract
Polycystic Ovarian Disorder (PCOD) is a prevalent endocrine illness in women of reproductive age which is a reproductive and metabolic disorder. It shows hormonal abnormalities in which there is an excessive production of androgens and that is one of the main causes of infertility, diabetes, irregular menstrual periods, hirsutism, hair loss, obesity and acne. One of the main features of PCOD is the presence of cysts on the ovaries, which can affect their ability to release eggs regularly and Anti-Müllerian hormone (AMH) plays an inhibitory role in follicular development and recruitment, contributing to follicular arrest. AMH inhibitory action on FSH-induced aromatase production likely contributes to hyperandrogenism in PCOD. Some factors which can cause of PCOD such as lack of exercise, skipping breakfast, fast food, unbalanced sleep, obesity, genetic, environmental factors and stress level. Lifestyle and nutrition can affect PCOD development and maintenance in PCOD can be done by lifestyle changes such as diet regulation (in taking of vitamins, antioxidant and Creatine) and exercise, as well as medications to regulate hormones, improve fertility and sleep which play a vital role in PCOD management.
***Keywords*:** PCOD, lifestyle changes, metabolic disorder**.**

Introduction

Polycystic Ovarian Syndrome (PCOS) is indeed a common endocrine disorder in women of reproductive age. It's characterized by hormonal imbalances, irregular menstrual cycles, and the presence of small cysts on the ovaries. In women without PCOS, the ovaries typically have a volume of around 4-6 ml each and are structured like a walnut, with a smooth surface. However, in PCOS, the ovaries can become enlarged and bulky, often exceeding 10 ml in volume [1]. This enlargement is due to the accumulation of multiple small follicles that may not mature properly, leading to hormonal disturbances and increased production of androgens (male hormones) such as testosterone. The hormonal imbalances seen in PCOS can result in a range of symptoms, including irregular periods, infertility, acne, excessive hair growth (hirsutism), and weight gain. Managing PCOS often involves a combination of lifestyle changes, medications to regulate hormones, and sometimes assisted reproductive technologies for those trying to conceive [2, 3]. In PCOS, the elevated levels of androgens, such as testosterone, can disrupt the normal ovulation process. Normally, during each menstrual cycle, several follicles begin to develop in the ovaries, but usually, only one follicle matures and releases an egg (ovulation). However, in PCOS, due to hormonal imbalances, multiple follicles may start to develop but often do not mature fully. This can lead to the formation of more than ten small follicular cysts in the ovaries each month [4]. In polycystic ovaries, there is a characteristic appearance of having more than 12 small follicles, typically measuring between 2 to 9 millimeters in diameter. These follicles often surround the periphery of the ovary, giving them a "pearl-necklace" appearance on ultrasound imaging [5].

The term "poly" in polycystic refers to "many," indicating the presence of numerous small follicles, while "cyst" refers to the fluid-filled sacs that these follicles form. These cysts are not the same as pathological cysts; rather, they are the result of the follicles not maturing properly and remaining as small sacs within the ovary. This accumulation of immature follicles is a key

characteristic of polycystic ovary syndrome (PCOS) and is one of the factors contributing to the hormonal imbalances and irregular ovulation seen in this condition [6]. Women with PCOS have a higher prevalence of subclinical atherosclerosis, which is the early stage of artery narrowing that can lead to cardiovascular events like heart attacks and strokes. This increased risk is often linked to factors like insulin resistance, dyslipidemia (abnormal lipid levels), and obesity commonly seen in PCOS. Obesity and insulin resistance are often central to the development and clinical manifestations of PCOS. Women with PCOS are more likely to experience psychological challenges such as depression and anxiety disorders. The hormonal imbalances, symptoms like irregular periods or unwanted hair growth, and the challenges of managing weight and associated health issues can all contribute to these psychological conditions [7]. This disorder is interrelated with hormonal imbalances, irregular menstrual periods and the presence of several small cysts on the ovaries [8].

In addition to impact on fertility, Polycystic Ovary Syndrome (PCOS) often produces itself a number of disturbing symptoms, some of which include excessive hair growth, acne, weight gain and mood changes. Stress reduction indeed plays a crucial role in managing PCOS symptoms because stress can exacerbate hormonal imbalances and lead to increased insulin resistance. The connection between PCOS, insulin resistance, and other health issues like obstructive sleep apnea and excessive daytime sleepiness is quite significant. It is the most common endocrine disorder of premenopausal women which is characterized by chronic oligoanovulation, hyperandrogenismand insulin resistance. Obstructive sleep apnea (OSA) and excessive daytime sleepiness (EDS) are strongly associated with insulin resistance and hypercytokinemia, independently of obesity [9]. The excessive production of male hormones, or hyperandrogenism, is a key feature of PCOS that can be linked to anovulation. Androgens, such as testosterone, can impact ovarian granulosa cells differently based on the stage of oocyte development and the surrounding environment [10]. This hormonal influence can affect early follicles, possibly contributing to the exaggerated growth seen in PCOS and the formation of multiple ovarian cysts. Androgens' actions on folliculogenesis can occur independently of follicle-stimulating hormone (FSH) during the initial phase of follicular development, known as recruitment. This suggests that androgens, along with other growth factors, play a role in the abnormal early follicular growth observed in PCOS [11].

However, women diagnosed with PCOS may suffer from several issues include Hirsutism, caused by elevated androgen levels, leads to excess hair growth on the body. Amenorrhea, or irregular periods, and menorrhagia, or heavy periods, are also prevalent in PCOS due to hormonal imbalances affecting the menstrual cycle. Skin problems like acne and oily skin are often associated with PCOS, along with hair-related issues such as hair loss and thinning on the scalp. Insulin resistance is another significant concern in PCOS, contributing to metabolic issues and weight-related problems like obesity. Fertility problems can arise due to irregular ovulation, while conditions like fibroids and endometriosis can compound pain and abnormal bleeding during menstruation for some individuals with PCOS [12,13].

Pathophysiology and etiology of PCOD

The pathophysiology of polycystic ovary syndrome (PCOS) is complex and involves multiple factors that interact to create the characteristic symptoms of the condition. While the exact cause of PCOS is not fully understood, several key mechanisms contribute to its development [14]. PCOS is associated with elevated levels of androgens (hyperandrogenism), such as testosterone, in the blood. This can lead to symptoms like hirsutism (excessive hair growth), acne, and male-pattern baldness. Many women with PCOS have insulin resistance, where their cells become less responsive to insulin [15]. This leads to higher insulin levels in the blood (hyperinsulinemia), which can further stimulate androgen production and disrupt ovarian function.The hormonal imbalances in PCOS can disrupt the normal menstrual cycle, leading to irregular or absent ovulation. This contriutes to infertility and difficulties in conceiving this process is known as anovulation.Follicles in the ovaries may fail to mature properly, leading to the formation of multiple small cysts. These cysts can be seen on ultrasound and are a characteristic feature of PCOS [16].

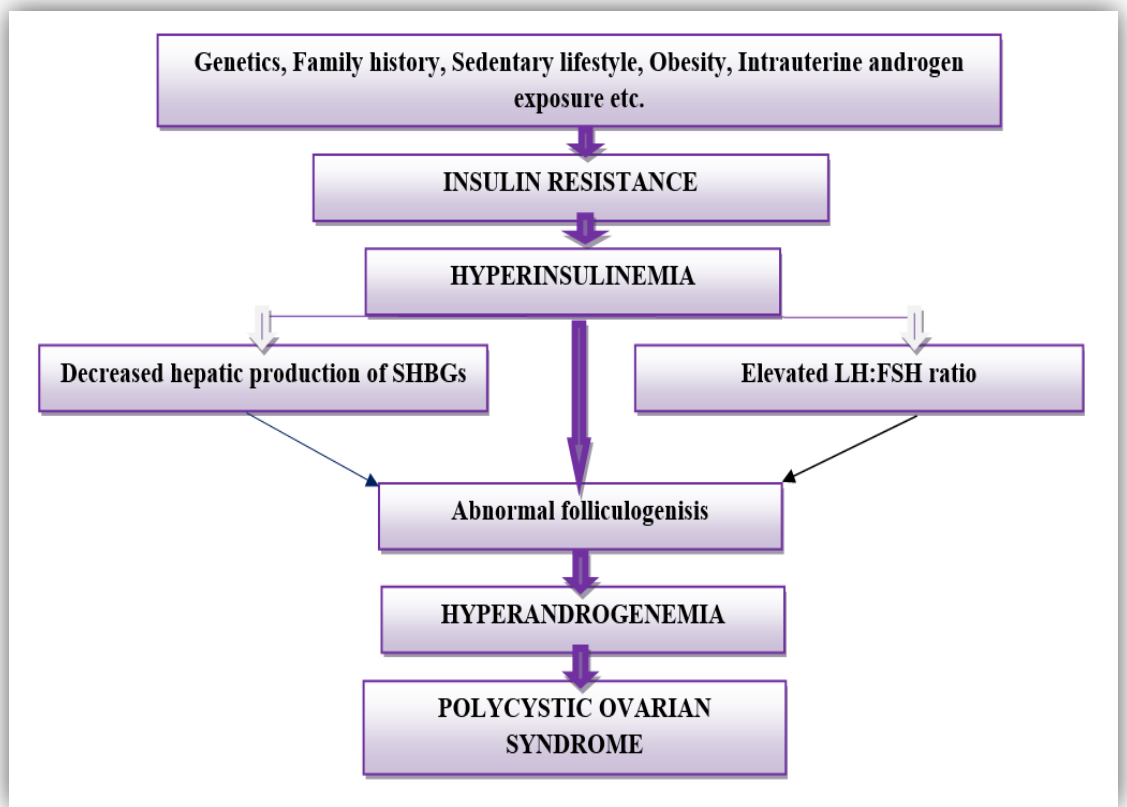

Fig.2 Pathophysiology of PCOS

FSH is essential for the development of ovarian follicles, particularly in the early stages of folliculogenesis. It stimulates the growth and maturation of follicles, promotes granulosa cell proliferation, and supports the production of estrogen by granulosa cells. In the context of polycystic ovary syndrome (PCOS), abnormalities in FSH secretion or sensitivity can contribute to the development of the condition [17]. Prolonged stimulation of FSH, such as with human chorionic gonadotropin (hCG), can lead to the formation of large ovarian cysts. This suggests a link between abnormal FSH signaling and the cystic nature of PCOS ovaries.FSH and its interactions with other regulatory proteins like follistatin and activin are critical for normal ovarian function and follicular development. Understanding these mechanisms can provide insights into the pathophysiology of PCOS and guide potential therapeutic approaches aimed at restoring hormonal balance and improving fertility outcomes [18]. Anti-Müllerian hormone (AMH) indeed plays a crucial role in reproductive development and folliculogenesis, and its dysregulation is implicated in conditions like polycystic ovary syndrome (PCOS). During embryonic development, AMH is secreted by Sertoli cells in males and granulosa cells in females. In males, AMH prevents the development of Müllerian ducts, which would otherwise form the uterus, fallopian tubes, and upper part of the vagina [19]. In females, AMH levels decrease after birth but remain elevated in the ovaries, where it regulates follicle development. In PCOS, AMH levels are typically elevated, reflecting the increased number of small antral follicles characteristic of the condition. This elevation in AMH levels is associated with various reproductive and metabolic/endocrine abnormalities seen in PCOS.AMH plays a important role in pathogenesis of PCOS by inhibit the recruitement and development of follicles and by inhibitory action on follicular development can lead to decreased aromatase production which converts androgen to estrogen [20].

Etiology

The etiology of polycystic ovary syndrome (PCOS) is complex and multifactorial, involving a combination of genetic, hormonal, metabolic, and environmental factors. Certain gene variants or mutations may predispose individuals to PCOS or contribute to its characteristic symptoms, such as hyperandrogenism and insulin resistance. Elevated levels of androgens (male hormones) are a hallmark feature of PCOS. This can lead to symptoms like hirsutism (excessive hair growth), acne, and male-pattern baldness [21].

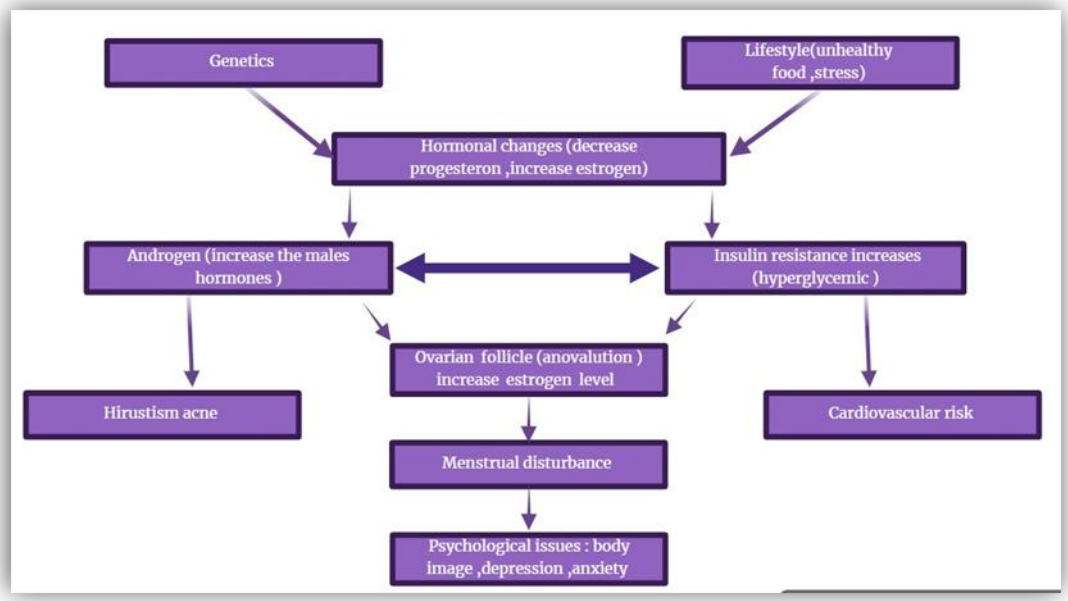

Fig.1 Etiology of PCOS

Lifestyle factors affecting PCOS

Stress

Hypothalamic-pituitary-adrenal (HPA) axis plays a crucial role in the body's stress response and is intimately linked with the regulation of menstrual function. The hypothalamus plays a central role in regulating the menstrual cycle through the release of gonadotropin-releasing hormone (GnRH). GnRH acts on the pituitary gland, specifically on cells called gonadotrophs, which are responsible for producing and releasing two important hormones: follicle-stimulating hormone (FSH) and luteinizing hormone (LH) [22]. FSH plays a crucial role in the ovarian cycle. In the early phase of the menstrual cycle, FSH stimulates the growth and development of follicles in the ovaries, while LH, which regulates estradiol secretion by the maturing follicle which is essential for ovulation and after ovulation helps in maintaining the corpus luteum [23]. Due to the disruption in this cycle, maintenance of regular menstrual function hindered or stops for some time; the hinderance and length of stop of menses basically depends on the continuation of the initiating physical, emotional or psychological stressful event. Stress can cause infertility; infertility causes stress as well! FHA is a condition characterized by the absence of menstrual periods (amenorrhea) due to excessive physical or emotional stress. The absence of ovulation and menstrual periods in FHA can contribute to infertility [23, 24].

Intake of junk food

Junk foods high in saturated fatty acids can contribute to inflammation and hormonal imbalances, including disruptions in progesterone metabolism during the luteal phase of the menstrual cycle. Progesterone is crucial for preparing the uterine lining for implantation and maintaining a healthy pregnancy if fertilization occurs. Imbalances in progesterone levels can lead to irregularities in the menstrual cycle and contribute to premenstrual symptoms [25]. Junk foods are often deficient in essential micronutrients like vitamin B6, calcium, magnesium, and potassium. These nutrients play important roles in hormonal regulation, neurotransmitter function, and overall health [25, 26].

Obesity

Adipose tissue, particularly in areas such as the breasts, abdomen, omentum (a fatty tissue layer covering abdominal organs), and fatty marrow of long bones, plays a role in converting androgens (male hormones) to estrogen through a process called aromatization. This conversion is mediated by the enzyme aromatase. Body weight influences the direction of estrogen metabolism. In very thin women, estrogen metabolism tends to produce a less potent, inactivated form of estrogen known as the 2-hydroxylated form.27 Conversely, in obese women, estrogen metabolism can lead to the production of more potent forms of estrogen, particularly the 16-hydroxylated form. This difference in estrogen metabolism can impact hormonal balance and function. Obese women may have a decreased capacity for estrogen binding with sex hormone-binding globulin (SHBG), a protein that binds to circulating hormones such as estrogen and testosterone; Adipose tissue can also serve as a storage site for steroid hormones, including estrogen, in obese individuals. This stored estrogen can contribute to overall estrogen levels in the body and influence hormonal balance [28].

Lack of physical activity

Irregular periods are strongly associated withdecreased levels of physical activity. Obesity and sedentary lifestyle can have a significant impact on hormonal balance, particularly affecting androgens and estrogens. Adipose tissue can act as a reservoir for lipid-soluble steroids like estrogen, which can disrupt normal hormonal levels. Additionally, obesity can alter the relationship between hormones and sex-hormone-binding globulin (SHBG), a protein that binds to and regulates the activity of sex hormones [29].

Skipping breakfast

Skipping breakfast has been associated with overweight and obesity globally. It can contribute to weight gain and metabolic issues like insulin resistance and elevated fasting lipid concentrations in adults. Breakfast plays a crucial role in regulating blood glucose levels, and fluctuations in blood glucose can affect cognitive function directly. Maintaining a balanced breakfast routine can help support healthy weight management and overall metabolic health [30].

Alcohol

Ovulatory infertility often involves hormonal imbalances, and the liver plays a critical role in metabolizing and excreting excess hormones from the bloodstream. When the liver is congested or overwhelmed, its ability to process hormones efficiently can be compromised. Alcohol consumption can further burden the liver, diverting its resources from hormone metabolism and excretion. This can exacerbate hormonal imbalances and contribute to ovulatory issues in women experiencing infertility [31].

Smoking

Smoking has wide-ranging effects on hormone levels and can disrupt various hormonal pathways in the body. The increased carbon monoxide content in the blood from smoking can inhibit hormone production over time. In the case of conditions like Polycystic Ovary Syndrome (PCOS), which is characterized by hormonal imbalances including elevated androgens, smoking can exacerbate symptoms due to its impact on androgen levels. These imbalances can lead to irregular periods, acne, excess hair growth (hirsutism), and other issues associated with PCOS [32].

Strategies to manage PCOS

Lifestyle management is often the first and crucial step in treating conditions like PCOS. Prioritizing physical and mental health can lead to a more fulfilling life in the long run. There are certain lifestyle management strategies, which work well in PCOS:

- Preventing obesity or managing weight can help improve hormonal balance and reduce symptoms associated with PCOS.
- Following a low-carbohydrate diet or making dietary changes based on individual needs can be beneficial. This may include focusing on whole foods, fiber-rich options, and balanced meals.
- Engaging in regular physical activity or exercise can help improve insulin sensitivity, manage weight, and promote overall well-being.
- Adopting healthy behaviors such as getting adequate sleep, managing stress, and avoiding smoking or excessive alcohol consumption can have a positive impact on PCOS symptoms.
- Incorporating stress-reducing techniques such as mindfulness, meditation, yoga, or seeking support from mental health professionals can contribute to a more stress-free lifestyle [33, 34].

Physical Activity

Regular physical activity, especially aerobic exercise, can indeed improve insulin sensitivity, enhance glucose metabolism, and contribute to overall health in various ways. The emphasis on exercise intensity over volume for health outcomes aligns with current research suggesting that the intensity of exercise can have a more significant impact on certain health markers. For PCOS specifically, exercise plays a crucial role in improving reproductive functions, reducing the risk of weight gain and metabolic syndrome, enhancing mental health, and promoting overall quality of life. While specific guidelines for the optimal exercise volume, intensity, and duration may vary depending on individual factors, aiming for at least 120 minutes of aerobic exercise per week can be a good starting point **[**35].

Sleep

In PCOD, sleep disturbances are commonly reported, and research suggests a link between these disturbances and mental health issues like anxiety and sadness. Additionally, reduced sleep duration is associated with increased risks of insulin resistance, obesity, and type 2 diabetes. The mechanisms linking sleep deprivation to insulin resistance may involve various pathways, including autonomic pathways and alterations in hunger hormones like ghrelin and leptin. Moreover, melatonin levels can be lower in individuals with PCOD, particularly in their follicular fluid. Melatonin receptors in the ovaries and its presence in intrafollicular fluid are involved in regulating sex steroid release during follicular development. Melatonin's

antioxidant properties also play a role in protecting ovarian follicles from damage. The circadian patterns of melatonin secretion, with levels peaking at night and decreasing during the day, are part of the body's communication of light-dark information. This contrasts with cortisol, which follows a different circadian pattern, peaking in the morning and decreasing during sleep, as it's regulated by the hypothalamic-pituitary-adrenal (HPA) axis [36,37].

Food Intake Management

The effects of lifestyle adjustment were studied in relation to the proportion of energy from macronutrients (protein, fat and carbs). The low glycemic index (LGI) diet, which emphasizes low-calorie, low-GI foods, has been linked to positive effects such as reduced fasting insulin, lower LDL cholesterol and triglycerides, and decreased waist circumference. On the other hand, high-GI diets (HGI) may not offer these benefits. Combining an LGI diet with omega-3 supplementation, physical exercise, and limits on punitive eating behaviors can further improve outcomes like increased HDL cholesterol, SHBG production, and body fat loss. Additionally, the ketogenic diet (KD), which prioritizes fat over carbs, has shown promise in addressing conditions like PCOS and fatty liver, leading to improvements in menstrual regularity, blood glucose levels, and weight reduction. A healthy eating approach involves consuming a variety of foods from different groups while minimizing processed foods, refined sugars, and unhealthy fats. Incorporating anti-inflammatory spices like turmeric, cinnamon, and fenugreek can also be beneficial for conditions like PCOS [38].

Vitamin D indeed plays a crucial role in various aspects of health, including calcium metabolism and bone health. The process of vitamin D activation through hydroxylation steps leading to calcidiol and eventually calcitriol highlights its role as a hormone rather than just a vitamin. This hormonal activity is believed to impact gene transcription, insulin metabolism, and fertility regulation, all of which are relevant in PCOS [39]. It's also worth noting the potential systemic consequences of vitamin D deficiency, extending beyond reproductive health to encompass chronic diseases like cancer, cardiovascular issues, autoimmune disorders, and psychological conditions such as depression and chronic pain. This underscores the importance of maintaining adequate vitamin D levels through supplementation when necessary, particularly in populations like women with PCOS who may benefit significantly from its effects on insulin sensitivity and hormonal balance [40].

Folate, or vitamin B-9, is indeed crucial for many metabolic processes, particularly DNA and RNA synthesis. Folic acid, the synthetic form of folate, has been linked to various health benefits, including improvements in glycemic control and reductions in inflammation and oxidative stress, especially in women with PCOS who are overweight or obese.41 PCOS is often associated with elevated homocysteine levels, which is a byproduct of methionine metabolism. Elevated homocysteine levels can have harmful effects on vascular endothelium, leading to conditions like atherosclerosis, thromboembolism, hyperinsulinemia, and ultimately cardiovascular disease. Therefore, managing homocysteine levels, possibly through adequate folate/folic acid intake, is crucial in mitigating these cardiovascular risks associated with PCOS. Overall, ensuring sufficient folate/folic acid intake, especially in higher doses when necessary, can be beneficial for women with PCOS in terms of metabolic health, insulin sensitivity, and cardiovascular risk management [42].

B-group vitamins, including B-1 (thiamine), B-6 (pyridoxine), and B-12 (cobalamin), are indeed crucial for processing homocysteine in the blood and preventing its harmful effects, particularly in the context of PCOS and insulin resistance.Good dietary sources of B-group vitamins include:

Thiamine (B-1): Nuts, seeds, whole grains, animal liver, fruits like oranges and avocados.

Pyridoxine (B-6): Eggs, legumes, milk, leafy vegetables, meats, broccoli, and mushrooms.

Cobalamin (B-12): Animal products such as meat, fish, eggs, and dairy products, as well as fortified foods like breakfast cereals [43].

Vitamin E, known for its antioxidant properties, plays a significant role in neutralizing free radicals and protecting cells from oxidative damage. In women with PCOS, vitamin E supplementation has shown potential benefits when combined with other nutrients like coenzyme Q10 or omega-3 fatty acids. Studies suggest that co-supplementation of vitamin E with coenzyme Q10 or omega-3 fatty acids can improve insulin resistance and reduce androgen levels in women with PCOS [44]. Alpha-tocopherol, the active form of vitamin E, is lipid-soluble and can activate intracellular antioxidant enzymes, acting as "radical scavengers" that protect cell membranes from lipid peroxidation. This mechanism underscores the importance of vitamin E in maintaining cellular health and function, especially in conditions like PCOS where oxidative stress and inflammation may play a role in pathogenesis [45].

Vitamin C, or ascorbic acid, is indeed a vital nutrient with potent antioxidant properties. It acts as a cofactor in essential enzyme reactions and plays a crucial role in maintaining overall health.In the context of PCOS, vitamin C has garnered attention as a potential therapeutic agent. It may contribute to improving ovarian morphology and addressing anovulation, a common issue in PCOS. Ascorbic acid's role in facilitating proper ovulation is notable, particularly its uptake during the pre-ovulatory phase. Additionally, vitamin C stimulates the production of progesterone and oxytocin, which are important hormones involved in reproductive processes [46].

Vitamin A, also known as retinol, is a crucial nutrient with roles in various aspects of health, including metabolic function and hormone production. In the context of PCOS, there is emerging research suggesting potential connections between vitamin A

and aspects of the disorder. One study involving women with PCOS looked at the impact of vitamin A supplementation on menstrual loss and found positive effects. Vitamin A is known to play a role in the growth and development of adolescents, which includes healthy endometrial growth [47].

Women with PCOS often exhibit lower levels of L-carnitine, which can potentially affect oocyte (egg) quality and contribute to insulin resistance and androgen-related issues commonly seen in PCOS. L-carnitine is synthesized in the body from the amino acids lysine and methionine. Its functions are diverse, including facilitating the transport of fatty acids into mitochondria for energy production, which is crucial for maintaining energy balance. Additionally, L-carnitine has been studied for its roles in carbohydrate metabolism and its potential to improve insulin resistance [48].

For women with PCOS, antioxidant supplementation has shown promise in improving insulin sensitivity, which is a key component of managing the condition. Additionally, antioxidants can support overall health by reducing oxidative stress and inflammation, both of which are often elevated in PCOS and can contribute to various health issues. Common antioxidants found in foods and supplements include vitamins C and E, beta-carotene, selenium, and polyphenols like flavonoids. Including a variety of antioxidant-rich foods in the diet, such as fruits, vegetables, nuts, seeds, and whole grains, can help support overall health and may have specific benefits for women with PCOS [49, 50].

ω-3 fatty acids, commonly found in fatty fish and fish oil, have a range of health benefits due to their anti-inflammatory, antithrombotic, antiarrhythmic, and antiatherogenic properties. These properties make them particularly interesting in the context of PCOS, a condition that involves insulin resistance and inflammatory factors.51 ω-3 fatty acids, can potentially improve PCOS by reducing insulin resistance and excess androgen levels.Incorporating ω-3 fatty acids into the diet or through supplementation may have beneficial effects on various aspects of PCOS, including hormonal balance, insulin sensitivity, and inflammation [52].

Magnesium is involved in various metabolic processes, including insulin signaling and glucose metabolism. Therefore, lower magnesium levels may contribute to insulin resistance, which is a common feature of PCOS. It's possible that optimizing magnesium intake through diet or supplementation could have benefits for managing insulin resistance and hormonal imbalances in women with PCOS, though further research is needed to fully understand this relationship [53].

Copper, while essential for various enzymatic functions in the body, can also contribute to oxidative stress by catalyzing the formation of ROS [reactive oxygen species] and decreasing glutathione levels the role of increased oxidative stress resulting from high generation of reactive oxygen species (ROS) in the pathogenesis of PCOS [54].

Current treatment options

Antiandrogen treatment

Flutamide is indeed an antiandrogen medication commonly used to treat conditions like hirsutism (excessive hair growth) and acne. It works by blocking the action of androgens, or male hormones, which can help reduce these symptoms in women. One crucial consideration with flutamide, especially when prescribed to women of reproductive age, is the risk of potential feminization effects on a male fetus if the woman becomes pregnant while taking the medication [55]. This is why contraception is often emphasized and deemed essential during flutamide treatment to prevent unintended pregnancy and potential harm to a developing male fetus. Regarding its effects on metabolic features in conditions like polycystic ovary syndrome (PCOS), studies have shown varying results. Some studies suggest a neutral effect of flutamide treatment on insulin sensitivity, while others indicate a mild positive effect, particularly among lean and obese PCOS patients [56].

Oral contraceptives

Oral contraceptive pills (OCPs) have long been a cornerstone in the management of polycystic ovary syndrome (PCOS). They are often prescribed to regulate menstrual cycles, reduce symptoms of hyperandrogenism (such as hirsutism and acne), and lower the risk of endometrial hyperplasia. OCPs work by providing a steady dose of synthetic hormones, typically estrogen and progestin, which can help regulate the menstrual cycle and suppress androgen production [57].

Statins

Statins have shown promise as an additional therapeutic option for addressing steroidogenic abnormalities in PCOS. They can inhibit the proliferation and steroidogenesis of ovarian theca-interstitial cells in women with PCOS. Statins can have potential fetal toxicity, effective contraception is essential when considering statin treatment in women of reproductive age who are not actively trying to conceive or are not using reliable contraception methods [58].

Clomiphene

It stimulates ovulation in women who have ovulatory disorders by inducing the release of hormones needed for ovulation. Clomiphene works by blocking estrogen receptors in the hypothalamus, which in turn prevents the brain from receiving the usual negative feedback signals. This lack of feedback leads to increased production of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the pituitary gland. These hormones are essential for the growth and maturation of ovarian follicles, ultimately promoting ovulation [59].

Metformin is a medication commonly used to manage type 2 diabetes, but it's also used off-label to treat conditions like polycystic ovary syndrome (PCOS) due to its effects on insulin sensitivity and glucose metabolism. Metformin primarily works by reducing the production of glucose in the liver (gluconeogenesis) and increasing the sensitivity of muscle and fat cells to insulin (insulin sensitivity). By doing so, it helps lower blood sugar levels and improve insulin resistance, which is a key factor in both diabetes and PCOS [60].

Spironolactone has anti-androgen properties, meaning it can block the action of androgens (male hormones) in the body. In conditions like PCOS where there is an excess of androgens, spironolactone can be beneficial. By reducing androgen levels, spironolactone can help improve symptoms such as acne, excessive hair growth (hirsutism), and hair loss (alopecia) in women with PCOS. Spironolactone works by blocking the effects of aldosterone, a hormone involved in regulating sodium and potassium balance in the body. By blocking aldosterone, spironolactone helps the body get rid of excess fluid while retaining potassium, hence its diuretic effect [61].

Letrozole

letrozole which is also known as Femara, works by inhibiting the aromatase enzyme. Which is responsible for converting male hormones (androgens) into female hormones (estrogens). Through this mechanism letrozole decreases the estrogen levels in the body. This can help slow down or stop the growth of estrogen-sensitive breast cancer cell [62].

Conclusion

In conclusion, adopting a holistic approach that includes lifestyle changes and nutrition interventions is essential for effectively managing PCOD. These interventions target underlying mechanisms such as insulin resistance, hormonal imbalances, inflammation, and weight management, ultimately improving symptoms and overall quality of life for women with PCOD. PCOD management should be individualized based on each woman's unique needs, symptoms, and health goals. Working with healthcare providers, such as endocrinologists, nutritionists, and physical therapists, can help develop personalized treatment plans that address specific aspects of PCOD. In addition to dietary changes, addressing other lifestyle factors such as stress management, adequate sleep, and regular physical activity is vital for comprehensive PCOS management. These lifestyle modifications can further support overall health and well-being, complementing the therapeutic approaches tailored to managing PCOS effectively.

Funding

There is no funding involve

Acknowledgement

Not Declared

Conflict of Interest

The authors have no conflict of interest

Informed Consent

No need of any informed consent in this paper

Ethical Statement

This review is following all the relevant ethical aspects

Author Contribution

All the authors have the equal contribution

References

1. El Hayek S, Bitar L, Hamdar LH, Mirza FG, Daoud GJFip. Poly cystic ovarian syndrome: an updated overview. 2016;7:124.
2. Gervásio CG, Bernuci MP, Silva-de-Sá MF, Rosa-e-Silva ACJdSJISRN. The role of androgen hormones in early follicular development. 2014;2014.
3. Balen AH, Morley LC, Misso M, Franks S, Legro RS, Wijeyaratne CN, et al. The management of anovulatory infertility in women with polycystic ovary syndrome: an analysis of the evidence to support the development of global WHO guidance. 2016;22(6):687-708.
4. Hafez E, Hafez BJRifa. Folliculogenesis, egg maturation, and ovulation. 2000:68-81.
5. KASE NGJD, DISORDERS MOO. Polycystic Ovarian Syndrome.337.

6. Narayan V. Ayurvedic Management of Polycystic Ovarian Disease with Chandraprabha Vati: Rajiv Gandhi University of Health Sciences (India); 2013.
7. Koneru A, S PJJoPH. Polycystic ovary syndrome (PCOS) and sexual dysfunctions. 2019;1(2):154-8.
8. Wild RAJS. Dyslipidemia in PCOS. 2012;77(4):295-9.
9. Lang CJ, Appleton SL, Vakulin A, McEvoy DR, Wittert GA, Martin SA, et al. Obstructive sleep apnea (OSA) and excessive daytime sleepiness (EDS) are independently associated with depression in a community based population of Australian men. 2015;191(C19):A3934.
10. Elsheikh M, Murphy C. Polycystic ovary syndrome: Oxford University Press; 2008.
11. Oduwole OO, Huhtaniemi IT, Misrahi MJIjoms. The roles of luteinizing hormone, follicle-stimulating hormone and testosterone in spermatogenesis and folliculogenesis revisited. 2021;22(23):12735.
12. Witchel SFJPE. Hirsutism and polycystic ovary syndrome. 2006:349-72.
13. Trüeb RM, Trüeb RMJTDHLPGtSMoA, Conditions R. The difficult dermatologic condition. 2015:49-137.
14. Zehravi M, Maqbool M, Ara IJIjoam, health. Polycystic ovary syndrome and infertility: an update. 2022;34(2):1-9.
15. Tsilchorozidou T, Overton C, Conway GSJCe. The pathophysiology of polycystic ovary syndrome. 2004;60(1):1-17.
16. Zeng X, Xie Y-j, Liu Y-t, Long S-l, Mo Z-cJCca. Polycystic ovarian syndrome: correlation between hyperandrogenism, insulin resistance and obesity. 2020;502:214-21.
17. Rimon-Dahari N, Yerushalmi-Heinemann L, Alyagor L, Dekel NJMmocdigd. Ovarian folliculogenesis. 2016:167-90.
18. Urbanek M, Legro RS, Driscoll DA, Azziz R, Ehrmann DA, Norman RJ, et al. Thirty-seven candidate genes for polycystic ovary syndrome: strongest evidence for linkage is with follistatin. 1999;96(15):8573-8.
19. Josso N, Belville C, Di Clemente N, Picard J-YJHru. AMH and AMH receptor defects in persistent Müllerian duct syndrome. 2005;11(4):351-6.
20. Garg D, Tal RJRbo. The role of AMH in the pathophysiology of polycystic ovarian syndrome. 2016;33(1):15-28.
21. Khan MJ, Ullah A, Basit SJTaocg. Genetic basis of polycystic ovary syndrome (PCOS): current perspectives. 2019:249-60.
22. Leistner C, Menke AJHocn. Hypothalamic–pituitary–adrenal axis and stress. 2020;175:55-64.
23. DITZEN B, LOUCKS TL, BERGA SLJIWsH. The role of Stress in Infertility. 2010;4:250.
24. Gard T, Noggle JJ, Park CL, Vago DR, Wilson AJFihn. Potential self-regulatory mechanisms of yoga for psychological health. 2014;8:100258.
25. Fujiwara T, Sato N, Awaji H, Nakata RJTOFSJ. Adverse effects of dietary habits on menstrual disorders in young women. 2007;1(1).
26. Akhila G, Shaik A, Kumar RDJIJoRiH, Pharmacy C. Current factors affecting the menstrual cycle. 2020;2(1):18-21.
27. Sanderson JT, Letcher RJ, Heneweer M, Giesy J, van den Berg MJEHP. Effects of chloro-s-triazine herbicides and metabolites on aromatase activity in various human cell lines and on vitellogenin production in male carp hepatocytes. 2001;109(10):1027-31.
28. Ko KM, Han K, Chung YJ, Yoon K-H, Park YG, Lee S-HJE, et al. Association between body weight changes and menstrual irregularity: the Korea National Health and Nutrition Examination Survey 2010 to 2012. 2017;32(2):248.
29. Orio F, Muscogiuri G, Ascione A, Marciano F, Volpe A, La Sala G, et al. Effects of physical exercise on the female reproductive system. 2013;38(3):305-19.
30. Thom G, Lean MJG. Is there an optimal diet for weight management and metabolic health? 2017;152(7):1739-51.
31. Chaudhary SA, Yogesh Manani YM, Archana Pithadiya AP, Pravin Masram PM, Krutika Joshi KJ, Satyavati Rathia SR. Modern life-style: a threat for the fertility. 20151Luciano AA, Lanzone A, Goverde AJJIJoG, Obstetrics. Management of female infertility from hormonal causes. 2013;123:S9-S17.
32. Ding H, Zhang J, Zhang F, Zhang S, Chen X, Liang W, et al. Resistance to the insulin and elevated level of androgen: A major cause of polycystic ovary syndrome. 2021;12:741764.
33. Gayathri K. A study to assess the effectiveness of lifestyle modification package on knowledge and attitude regarding weight reduction among women with pcos at janet nursing home, Trichy: Our Lady of Health College of Nursing, Thanjavur; 2015.
34. Hoeger KMJCo, gynecology. Obesity and lifestyle management in polycystic ovary syndrome. 2007;50(1):277-94.
35. Butt MS, Saleem J, Zakar R, Aiman S, Khan MZ, Fischer FJBPH. Benefits of physical activity on reproductive health functions among polycystic ovarian syndrome women: a systematic review. 2023;23(1):882.
36. Olcese JMJFie. Melatonin and female reproduction: an expanding universe. 2020;11:515354.
37. Terzieva DD, Orbetzova MM, Mitkov MD, Mateva NGJFM. Serum melatonin in women with polycystic ovary syndrome. 2013;55(2):10.
38. Shrestha A, Dixit A, Zaidi AJJoF, Sciences N. Assessment of lifestyle and diet modification of patients suffering from polycystic ovarian disease (PCOD) in North India. 2019;7(4):60-5.
39. De Leo V, Musacchio M, Cappelli V, Massaro M, Morgante G, Petraglia FJRB, et al. Genetic, hormonal and metabolic aspects of PCOS: an update. 2016;14(1):1-17.
40. Gottfried S, Hamrick K. Vitamin D and Polycystic Ovary Syndrome (PCOS)| Blog| Metagenics.

41. Fatahi S, Pezeshki M, Mousavi S, Teymouri A, Rahmani J, Varkaneh HK, et al. Effects of folic acid supplementation on C-reactive protein: A systematic review and meta-analysis of randomized controlled trials. 2019;29(5):432-9.
42. Fonseca V, Guba SC, Fink LMJEr. Hyperhomocysteinemia and the endocrine system: implications for atherosclerosis and thrombosis. 1999;20(5):738-59.
43. Sharma Ghimeray P. Impact of Age, Meal, Diet and Digestive Discomfort on B-Vitamin Bioavailability: ResearchSpace@ Auckland; 2021.
44. Irianto CB, Prasetyadi EGJCDK. Coenzyme Q10 and/or Vitamin E Supplementation for Polycystic Ovarian Syndrome. 2021;48(11):361-4.
45. Begum MS, Areen S. Optimizing Polycystic Ovarian Disorder (PCOD) Treatment with Personalized Lifestyle and Nutrition Strategies. 2023.
46. Sengupta P, Dutta S, Hassan MFJJoIS, Technology. Polycystic ovary syndrome (PCOS) and oxidative stress. 2024;12(3):752-.
47. Büyükgebiz A, Böber E, Büyükgebiz BJJoPE, Metabolism. Vitamin A and beta carotene levels in constitutional delay of growth and puberty. 1997;10(1):51-4.
48. Skoracka K, Ratajczak AE, Rychter AM, Dobrowolska A, Krela-Kaźmierczak IJAin. Female fertility and the nutritional approach: the most essential aspects. 2021;12(6):2372-86.
49. Meera B, Muralidharan P, Hari RJJoH, Spices, Plants M. Antioxidant potential of Caesalpenia bonducella seeds in the management of polycystic ovary syndrome (PCOS) using mifepristone induced rats model. 2021;27(2):123-34.
50. Hussain A. To Explore the Insilico Potential of Olea Europaea Fruit for Drug Development in PCOS: CAPITAL UNIVERSITY; 2022.
51. Raja-Khan N, Stener-Victorin E, Wu X, Legro RSJAJoP-E, Metabolism. The physiological basis of complementary and alternative medicines for polycystic ovary syndrome. 2011;301(1):E1-E10.
52. Huang Y, Zhang XJM. Meta-analysis of the efficacy of ω-3 polyunsaturated fatty acids when treating patients with polycystic ovary syndrome. 2023;102(39):e35403.
53. Luo X, Cai W-Y, Ma H-L, Cong J, Chang H, Gao J-S, et al. Associations of serum magnesium with Insulin resistance and testosterone in women with polycystic ovary syndrome. 2021;12:683040.
54. Galli F, Piroddi M, Annetti C, Aisa C, Floridi E, Floridi AJCdih. Oxidative stress and reactive oxygen species. 2005;149:240-60.
55. Hejmej A, Kotula-Balak M, Bilińska BJSCA. Antiandrogenic and estrogenic compounds: effect on development and function of male reproductive system. 2011:57-9.
56. Luque-Ramírez M, Ortiz-Flores AE, Nattero-Chávez L, Escobar-Morreale HFJEOoDS. A safety evaluation of current medications for adult women with the polycystic ovarian syndrome not pursuing pregnancy. 2020;19(12):1559-76.
57. Vrbikova J, Cibula DJHru. Combined oral contraceptives in the treatment of polycystic ovary syndrome. 2005;11(3):277-91.
58. Rashidi B, Abediasl J, Tehraninejad E, Rahmanpour H, Sills ESJJoIM. Simvastatin effects on androgens, inflammatory mediators, and endogenous pituitary gonadotropins among patients with PCOS undergoing IVF: results from a prospective, randomized, placebo-controlled clinical trial. 2011;59(6):912-6.
59. Mannava LL. A Comparative Study on Ovulation Induction with Clomiphene Citrate Versus Letrozole in Women with Infertility: A Prospective Randomized Trial at Infertility Clinic, KVG Medical College and Hospital Sullia: Rajiv Gandhi University of Health Sciences (India); 2020.
60. Viollet B, Guigas B, Garcia NS, Leclerc J, Foretz M, Andreelli FJCs. Cellular and molecular mechanisms of metformin: an overview. 2012;122(6):253-70.
61. Somani N, Sawaya MJCDDT. Antiandrogens and Androgen Inhibitors. 2019;4.
62. Pilutin A, Misiakiewicz-Has K, Kolasa A, Baranowska-Bosiacka I, Marchlewicz M, Wiszniewska BJFHeC. The immunoexpression of androgen receptor, estrogen receptors alpha and beta, vanilloid type 1 receptor and cytochrome p450 aromatase in rats testis chronically treated with letrozole, an aromatase inhibitor. 2014;52(3):206-17.