International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 33-42 www.ijprajournal.com ISSN: 2456-4494

Polycystic Ovary Syndrome: A Comprehensive Review of Its Clinical Presentation, Comorbidities, Long-Term Complications and Management

Aleena Jose[1*], Anuja S Babu[2*], Sampoornna S[3*], Sreekutty S[4*], Alphonsa Mathew[5*]

[1*,2*,3*,4*]*Bpharm students of Indira Gandhi Institute Of Pharmaceutical Sciences, Perumbavoor,Ernakulam, Kerala*

[5*]*Associate professor, Department of pharmacy practice, Indira Gandhi Institute Of Pharmaceutical Sciences, Perumbavoor, Ernakulam, Kerala*

Date of Submission: 01-03-2025 Date of Acceptance: 10-03-2025

ABSTRACT:
Polycystic Ovary Syndrome is a common hormonal and metabolic disorder that affects many women of reproductive age and can lead to symptoms of irregular menstruation, hirsutism, acne, and weight gain. It can also contribute to health problems such as insulin resistance,obesity, type 2 DM, and fertility problems. PCOS is a multifaceted condition based on hormones, genetics, and metabolic factors and associated with long-term risks such as heart disease, endometrial cancer, and mental health challenges, including anxiety and depression. Diagnosis follows established guidelines, includinga medical history, hormone tests, and ultrasound scans. PCOS is considered to be a not alleviated disorder, but PCOS can be managed by lifestyle changes, medication such as birth control pills and metformin, or when wishing to conceive, fertility treatments are advised. The early detection of the disorder will be better for the improved lifestyle of the females who are diagnosed with PCOS, and they can shift to a healthier life by diet, exercise, and by undertaking treatment.

KEYWORDS: PCOS, insulin resistance, comorbidities, Rotterdam criteria, CVD, endometrial cancer, lifestyle modifications.

I. INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a reproductive and dysmetabolic syndrome manifested by elevated male hormonal levels, “amenorrhea”, “oligomenorrhea”,irregular menstruation,multiple cysts in ovary,obesity,acne,“hypertension”,diabetes,malepat tern hair growth,and infertility [1][2].40 percent of women with PCOS have resistance to insulin,which leads to development of type 2 diabetes[3].The data suggested by WHO says that about one hundred sixteen million of women are affected with PCOS globally[2][4].Eventhough PCOS starts with menarche,most of the PCOS affected women are of age between twenty and thirty.PCOS in adolescent girls are mostly not diagnosed and less reported [5].If not diagnosed,PCOS affected women may developinfertility,metabolic disorders and cardiovascular diseases and uterinecancers [2].

PCOS affects 2% to 8% of women of reproductive age between 18 to 45 years worldwide. The prevalence of PCOS in India is between 2% to 35%. PCOS is associated to avariety of “metabolic-related conditions such as obesity, metabolic syndrome,NAFLD and abnormalities in blood sugar levels”[6].

II. PATHOPHYSIOLOGY

The precise pathophysiology of PCOS and the event that causes it are still unknown. Nonetheless, a number of biochemical anomalies have been identified, and correlations and connections between them have been established. Numerous of these anomalies feed off one another in vicious cycles[12]

Hypothalamic pituitary

FSH is low-normal while LH is elevated. A higher frequency and amplitude of pulses in PCOS augment the normal episodic secretion of LH, whereas FSH is either muted or remains unaltered. Consequently, even throughout the ovulatory cycles, LH levels may increase and the LH is to FSH ratio may increase to more than 2.5. However, up to 10% to 20% of women with PCOS may have these numbers as normal[13].

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 33-42 www.ijprajournal.com ISSN: 2456-4494

Hyperandrogenism

Every PCOS patient has heightened androgen sensitivity. Up to 70% have elevated levels, while the remaining 30% fall within the high-normal range. Three main androgens are in circulation. They are androstenedione (of which the ovaries generate more than 90%),testosterone (made equally by the ovaries and adrenal glands) and DHEA-S (mostly generated in the adrenal glands)[14] .

Insulin resistance and hyperandrogenism

A significant portion of women having PCOS, regardless of race, have IR, if they have BMI of more than twenty-five. The key question in PCOS is whether hyperandrogenism or hyperinsulinemia causes the other, as the two conditionscoexist.Undoubtedly, hyperandrogenism,whether exogenous or tumorous, can lead to increased insulin levels and glucose intolerance. Acanthosis and insulin resistance are improved by reducing such hyperandrogenism. Several mechanisms could account for this connection. Insulin can boost androgen production in a number of ways. By engaging with either its own receptor or the IGF-1 receptor, it directly may boost androgen production in the ovary by raising the activity of the P450 c17-alpha enzyme. As previously mentioned, it may modify the ovarian response to LH in addition to causing or exacerbating the abnormal LH secretion observed in PCOS. Additionally, it inhibits the liver's synthesis of SHBG, which raises the levels of free testosterone. Therefore, either by boosting intraovarian androgens, changing gonadotropin release, or directly affecting the ovary, insulin modifies normal folliculogenesis.[12]

III. SYMPTOMS

Patients with PCOS may develop symptoms of irregular menstrual cycle, "amenorrhea",increased androgen level,acne,male pattern hair growth,hair loss and presence of polycystic ovaries.It may also show presence of metabolic disturbances including insulin resistance and increased cholesterol level[7][10].It was found that over past twenty years,metabolic,cardiovascular,reproductive risks such as fertility issues are occurring most frequently[8].High prevalence of moderate to severe depression and anxiety also have been found in PCOS patients[9][11].

IV. DIAGNOSIS

Mainly, the diagnosis for PCOS condition is not well defined.[15] The polycystic ovarian syndrome is analyzed by physicians using the Rotterdam and Amsterdam criteria. The ultrasound scanning is used to determine the growth of cysts in the ovaries. The basic diagnosis tests that need to be performed by assessing the complete medical history of the suspect, physical examinations need to be done along with blood tests, pelvic ultrasound, biopsy, etc. [15][16]

The NIH criteria were sponsored for clinical study technique for diagnosis of PCOS in participants, and the study received features of biochemical evidence on HA and OD, the secondary causes were excluded from the study[17].

The Rotterdam criteria mention that two out of three phenotypes need to be diagnosed to confirm PCOS and identify PCOM as a diagnostic technique. AES criteria mentioned that three of the four phenotypes need to be diagnosed. Further studies introduced new guidelines for diagnosing the PCOS in participants[17].The high androgen levels, oligomenorrhea, hirsutism, etc., diagnosis will enhance the validation, increase accuracy [16].
The signs and symptoms which we can identify are mentioned in Table 1.1[16]

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 33-42 www.ijprajournal.com ISSN: 2456-4494

SIGNS AND SYMPTOMS FOR DIAGNOSING PCOS
Ovaries are enlarged with enormous cysts.
Irregular menstruation[anovulation/oligo-ovulation]
Abdominal pain
Acanthosis Nigricans
Acne /skin tags
Alopecia
Hirsutism/Male Pattern Hair growth
Hyperandrogenism

Transvaginal exams and ultrasound scanning were the primary sonographic methods included in the Rotterdam criteria, and while they are accurate in detecting PCOS, the approach is overused, and incorrect interpretations are also happening[18].

Once the PCOS diagnosis has been over, some problems may arise in the suspects like "MI, risk of Diabetes, endometrial cancer, dyslipidaemia, HTN, anxiety, depression, etc." Mostly reported cases shows issues like "gestational diabetes, miscarriages, premature delivery, pre-eclampsia"[16].

V. COMORBIDITIES ASSOCIATED WITH PCOS

Polycystic ovarian syndrome is caused by several comorbidities and complications, which affect the health status of women at the reproductive age group[19][20]. Some of the comorbidities observed are:

- Metabolic Comorbidities
- Cardiovascular Comorbidities
- Reproductive Comorbidities
- Hormonal Comorbidities
- Physiological comorbidities

The PCOS diagnosis excluded some of the phenotype impersonate disorders and some of the comorbidities included are mentioned in Table 1.2, and thyroid function tests are excluded[21].

Even though theoretically PCOS did not be linked to thyroid dysfunctions like hyperthyroidism or hypothyroidism, but some research suggests that they are linked. Many studies have explored how common thyroid issues are in people with PCOS, including conditions like "autoimmune thyroiditis, SCH, Graves' disease, thyrotoxicosis, thyroid nodules, nodular goitre and even thyroid cancer." Understanding these connections could help in better diagnosing and managing both conditions together[21]

Thyroid cancer is the most common endocrine cancer and is three times more common in women than in men. Some evidence suggests a possible link between PCOS and thyroid cancer, but research is limited. Most studies focus on thyroid nodules rather than cancer, and no direct

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 33-42 www.ijprajournal.com ISSN: 2456-4494

epidemiological studies confirm the risk in PCOS patients yet[21][22].

The list of comorbidities in Table 1.2 summarizes the comorbidities occurring in the specified category[19][20].

SI NO	CATEGORY	COMORBIDITIES
1	METABOLIC	Insulin resistance Type 2DM Obesity Dyslipidemia NAFLD
2	CARDIOVASCULAR	Hypertension Stroke Heart Disease
3	REPRODUCTIVE & HORMONAL	Infertility Cancer Endometrial Hyperplasia
4	PSYCHOLOGICAL	Depression Anxiety Eating disorders [binge eating & emotional eating risk will increase]
5	OTHERS	Autoimmune conditions OSA/sleep apnea

VI. LONG-TERM COMPLICATIONS OF PCOS

Cardiovascular risk

The primary cause of women having PCOS's elevated risk of heart disease appears to be elevated insulin levels.There is pancreatic beta-cell dysfunctionin the absence of decreased glucose tolerance, which is negatively linked with the quantity of SHBG. This results in testosterone excess,persistent unobstructed estrogen release. IR in PCOS considerably raises the risk of heart problems in these individuals by two processes. Direct atherogenic activity is one way, and the negative impact of the lipoprotein profile[23]is another. Angiographyshows more widespread CAD in women having PCOS [24].Diabetes brought on by PCOS and IGT are recognized risk factors for CVD.Women having PCOS have a markedly altered lipid panel. Serum TAG, total $C_{27}H_{46}O$, and LDL cholesterol are typically elevated in them[25]. Conversely, there is a reduction in HDL levels, namely the HDL-2 subfraction [26][27]. Furthermore, there is an increase in systemic plasminogen in activator inhibitor-I concentrations [28]. The latter may result in decreased fibrinolysis, which would directly impact lymphatic vessel and cause changesassociatedwithCHD [29]. Thus, there is growing evidence that women having PCOS are in fact at higher risk of CVD. "Pre-eclampsia is four times more common inobese women with PCOS who become pregnant than in the general pregnant population"[30].Warning signs for atherosclerotic conditions, increase in blood pressure, MI appear to developearlier in life in women with PCOS than in those without[31][32].

Endometrial cancer

The syndrome's characteristic prolonged anovulation is thought to be the primary mechanism causing the ongoing, unregulated release of estrogens and, as a result, an elevated risk of endometrial carcinoma[33][34]."Obesity, long-term use of estrogens, nulliparity, infertility, hypertension, and diabetes" are known to enhance the risk of endometrial carcinoma[35]. It is recognized that the most of these factors are also associated to PCOS. "Adenocarcinoma may develop from endometrial hyperplasia".Eventhough it is nearly hard to pinpoint the exact rate of progression, it is anticipated that eighteen percent of "adenomatous hyperplasia cases" will develop into carcinoma during the next two to ten years[36]. Periods longer than three months may be associated with

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 33-42 www.ijprajournal.com ISSN: 2456-4494

endometrial intra-epithelial neoplasia and subsequent carcinoma in women diagnosed with PCOS[31][37].

Ovarian Cancer

A doubling of androgen situations during gestation is associated with a 40 – 50 increased threat of frame serous and invasive mucinous excrescences [38] although studies of pre-diagnostic androgen situations not during gestation have been mixed [39]. Nine studies have examined the association with ovarian cancer threat to date [40]. PCOS has been believed to increase ovarian cancer threat through increased androgen exposure [41].Four of these investigations included 12 or fewer instances of ovarian cancer, indicating that several of these studies had inadequate power [42][43]. The danger of ovarian carcinoma in women with no ovulation has been the subject of much discussion and worry, especially due to the widespread use of ovulation inducing medication in these individuals. There may be anassociation between PCOS and a higher risk of ovarian carcinoma,as per multiple lines of evidence [44]. Earlypuberty, late -onset menopause, and nulliparous (many ovulations) women seem to be at higher risk. It is possible that triggering numerous ovulations in infertile women will increase their risk, although there is no proof to support this idea [45]. Therefore, despite the fact that women having PCOS are thought to be in alower risk group for ovarian carcinoma because of their lifetime decreased rate of ovulation, an imbalance in their risk for ovarian cancer will theoretically be created by using ovulation induction treatments and inducing multi-follicular ovulations [46][31].

Breast cancer

Infertility, obesity, and hyperandrogenism are characteristics that have been linked to the occurrence of breast cancer [23][31]. However, research hadn't any significant increase in the frequency of breast cancer in PCOS afflicted women. However, there appears to be a favourable correlation between PCOS and having a background of breast cancer. In a research including two hundred and seventeen women, the percentage of women having a positive background of breast cancer was considerably greater among PCOS afflicted women than among controls [47]

Infertility

Individual differences in the specific clinical manifestations are significant[48].Menstrual difficulties, infertility, insulin resistance (IR), metabolic diseases, and varied degrees of psychosocial issues and a lower quality of life are all common in PCOS patients [49][50]. Ovulation problems are a common feature of infertile people with polycystic ovarian syndrome. Infertility appeared to be influenced by a number of PCOS comorbidities. Specifically, obesityand insulin resistance (IR) were linked independently to lower pregnancy and live-birth rates as well as an increased risk of abortion[51][52]. Women with PCOS have also been found to have endometrial abnormalities, which may have an impact on implantation. Lastly, ovarian changes were characterized "at multiple levels, including ovarian/follicular/corpusluteumvascularityfollicular fluid environment [53]and the competence[47] and quality of the resulting oocytes". According to the most recent recommendations of the Task Force of Experts[38], which was formed by the "Endocrine Society", PCOS is only a risk factor for infertility when "oligoanovulation" is present. As a result, they advised that all women with PCOS who are trying to conceive should have their menstrual history checked for ovulatory status [54].

VII. TREATMENT AND MANAGEMENT OF PCOS

PCOS treatments must be customized for each patient; treatment objectives might involve reducing "hyperandrogenic" signs, triggering menstrual cycle, controlling periods,avoiding "cardiometabolic" difficulties[55]. The most upsetting symptoms for women having PCOSinclude infertility, excessive hairiness,irregular menstruation. Because "PCOS" has a complicated etiology, treatment is rarely monotherapeutic instead, it is customized to the patient's specific indications and symptoms. For the management and treatment of PCOS, a variety of complementary therapies have been proposed. The cornerstone of managing PCOS is thought to be modifications to one's diet and lifestyle. To alleviate the most common symptoms of PCOS, including periods that are irregular, androgen-related symptoms, and "anovulation" that causes infertility, various pharmacological and non-pharmacological treatments can be employed. There are many therapeutic options that may be useful for controlling metabolic comorbidities in PCOS, but it's important to recognize have no one treatment is appropriate may completely address the variety of insulin resistance syndrome in women have PCOS[56].

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 33-42 www.ijprajournal.com ISSN: 2456-4494

PHARMACOLOGICAL MANAGEMENT

Oral Contraceptives and Anti-Androgens

Acne and "hirsutism" in PCOS-afflicted women. OCs work by promoting a negative feedback loop on LH secretion, which lowers "hyperandrogenism" and the ovaries synthesis of androgen [57]. They decrease blood levels of free androgens and increase SHBG generated by the liver. Additionally, OCs function by binding DHT to androgen receptors, preventing the peripheral conversion of testosterone to DHT, and reducing the release of adrenal androgens. The dosages and drug combinations of OC preparations can affect their risk-benefit ratios. Anti-androgens, such as "finasteride", "flutamide", CPA, and "spironolactone", are used to treat" hyperandrogenism" because they consistently reduce androgen levels. In order to address "hirsutism" and other androgen-related problems, androgen antagonist are commonly used the drugs in PCOS. Androgen antagonist receptor medications that shows promise in curing the symptoms of PCOS. Due to its effects on the pituitary and brain, as well as ovarian steroidogenesis, the primary outcome of utilizing OCs is a reduction in "hyperandrogenism". Owing to these characteristics, it is a pharmacologically successful treatment for "hirsutism", acne, irregular menstruation, and androgenic alopecia associated with "PCOS". It has been demonstrated that "flutamide", the most common competitive antagonist of ARs, helps women with "PCOS" by lowering "hirsutism" and acne. "Improved ovulation and menstrual cycle regularity" were also reported by "PCOS" patients on" flutamide" therapy. Furthermore, "flutamide" treatment enhanced the lipid panels of PCOS women, resulting in a significant reduction in total cholesterol, LDL, and TGs, independent of weight changes, in both obese and lean PCOSwomen. All things considered, research on the use of "anti-androgenic" drugs, either alone or in combination, in PCOS patients has demonstrated that the targeted decrease in" hyperandrogenism" and, by extension, androgenic activity, has a favorable impact, improving a number of "PCOS" characteristics. Women with" PCOS" should undergo thorough screening to determine risk factors for serious OC side effects, including a history of smoking, obesity and hypertension, and a history of clotting problems, to name a few crucial variables[4].

Metformin

For "PCOS" individuals with "DM2" or "IGT" who are unable to change their lifestyle, the Endocrine Society advises beginning "metformin". It reduces the rate at which 'IGT" leads to "DM2". Additionally," metformin" improves vascular indicators, irregular waist-to-hip ratios, and menstrual periods in non-obese women with PCOS. For patients who are not candidates for hormonal contraceptives, "metformin" is also a second-line treatment for irregular menstruation. It helps restore regular menstruation, lower insulin resistance, and aid in weight loss. It is frequently used in teenage "monotherapy". While it can somewhat alleviate the symptoms of androgen excess, it should not be used primarily to treat clinical "hyperandrogenism"[20].

Clomiphene citrate

As percurrentguidelines, CC may be used as the first choicemedication for PCOSafflicted women who experience "anovulatory infertility". CC is an effective estrogen modulator that is inexpensive, safe, and easy to administer and monitor. Higher ovulation and pregnancy rates were obtained with anextended CC regimen compared to "gonadotropin"-induced ovulation, indicating that a longer duration of CC administration may be better for CC-resistant 'PCOS" patients. Newly suggested CC administration procedures include luteal phase and stair-step regimens. Ovulation and pregnancy rates were increased by administering 100 mg of CC daily during the luteal phase, even though the total number of follicles during stimulation was significantly higher. In CC-resistant women, the stair-step strategy, which involved taking 50 mg CC for five days and then increasing the dosage every week if there was no ovarian response, up to 150 mg daily, was less time-consuming and more effective in terms of ovulation rate[58].

Calcium and Vitamin D Supplements

By changing "AMH signaling", "FSH sensitivity" and progesterone synthesis in human granulose cells, vitamin D contributes physiologically to reproduction, which involves ovarian follicular growth and "luteinization". It also affects glucose homeostasis through a number of mechanisms. Some possible effects of vitamin D on glucose homeostasis include the presence of a particular VDR in skeletal muscle and pancreatic cells, the expression of the enzyme 1-hydroxylase and the presence of a vitamin D response element

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 33-42 www.ijprajournal.com ISSN: 2456-4494

in the human insulin gene promoter. In addition to raising the risk of CVS disease, low 25(OH)D levels may exacerbate "PCOS" symptoms such "insulin resistance", irregular menstruation and "ovulation", infertility, "hyperandrogenism", and obesity. "Vitamin D supplementation" can lower unusually high blood AMH levels in vitamin-D-deficient PCOS patients and increase serum anti-inflammatory soluble receptors for advanced glycation end products. Specifically, supplementing with vitamin D and calcium along with metformin medication may help PCOS patients with follicular development, ovulation, hyperandrogenism, and regular menstruation. High levels of AMH in PCOS-afflicted women cause abnormal ovarian folliculogenesis. Serum AMH levels are restored by vitamin D therapy, which could result in better folliculogenesis [4].

NON-PHARMACOLOGICAL MANAGEMENT

Weight loss, exercise and lifestyle interventions

In an evidence-based approach, changing one's lifestyle is the first choice medication for the majority of overweight PCOSwomen. Additionally, it is important to prevent excessive weight gain in all women having PCOS, without considering their baseline weight[59]. Significant clinical advantages can be obtained with as low as 5% to 10% weight loss, which improves metabolic characteristics, psychological results, and reproductive characteristics. Research indicates that even if women continue to be overweight or obese, changing their lifestyles with modest, attainable goals might have positive therapeutic effects. Nutritionally adequate, low fat moderate protein, and high carbohydrate intake with increased fiber-rich wholegrain breads, cereals, fruits, and vegetables, along with moderate regular exercise, are the standard dietary management of obesity and related 'comorbidities'. Over the course of six to twelve months, a moderate energy reduction diet (500 to 1,000 kcal/day reduction) reduces body weight by 7% to 10%. Targeting fruit juice, soft drinks, portion sizes, and high-fat foods are easy and useful ideas that may be discussed in a few minutes during a medical visit. Like the general population, exercise objectives should be centered on the advantages to overall health rather than weight loss[60]. It is currently unclear whether certain dietary strategies are better than calorie restriction alone, and further study is required. Certain dietary strategies have been proposed for PCOS, such as "low-carb", low-protein, and low-"glycaemic" index/"glycaemic" load diets. According to the available data, a variety of dietary approaches can also enhance weight, as well as reproductive and metabolic characteristics in PCOS, provided that they are safe, nutritionally sufficient, and long-lasting[60][61].

VIII. CONCLUSION

The reproductive and dysmetabolic syndrome known as polycystic ovary syndrome (PCOS) is characterized by high levels of male hormones, irregular menstruation, a number of ovarian cysts, obesity, acne, hypertension, diabetes, male pattern hair growth, and infertility.Early identification and personalized treatment can mitigate symptoms and reducing long-term complications and increase the quality of life. Comorbidities like diabetes mellitus, thyroid,increased cholesterol level, increased blood pressure, glucose tolerance may lead to long term complications like CVD,endometrial cancer,ovarian cancer and infertility. Lifestyle interventions help in the management of PCOS.Clomiphene citrate and metformin are the first choice of drugs used in the treatment of PCOS.

REFERENCE

[1]. Amale P, Deshpande S, BarethiaV.Understanding status of PCOS in Nagpur city: Asurvey-based study.Indian Journal of Pharmacy and Pharmacology. 2019 Jul-Sep;6(3):93-98.

[2]. Jabeen A,YaminiV,Rahman Amberina A, Dinesh Eshwar M, Vadakedath S, Begum GS, Kandi V. Polycystic Ovarian Syndrome: Prevalence, Predisposing Factors, and Awareness Among Adolescent and Young Girls of South India.Cureus.2022Aug;14(8).

[3]. Liao WT, Huang JY, Lee MT, Yang YC, Wu CC. Higher risk of type 2 diabetes in young women with polycystic ovary syndrome: A 10-year retrospective cohort study. World J Diabetes. 2022 Mar 15;13(3):240-250.

[4]. Singh S, Pal N, Shubham S, Sarma DK, Verma V, Marotta F, Kumar M. Polycystic Ovary Syndrome: Etiology, Current Management, and Future Therapeutics. J Clin Med.2023;12:1454.

[5]. Meczekalski B, Niwczyk O, Kostrzak A, Maciejewska-Jeske M, Bala G, Szeliga A. PCOS in Adolescents-Ongoing Riddles in

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar – Apr 2025, pp: 33-42 www.ijprajournal.com ISSN: 2456-4494

Diagnosis and Treatment. J Clin Med. 2023 Feb 3;12(3):1221.

[6]. GanieMA, Chowdhury S, Malhotra N, et al. Prevalence, Phenotypes, and Comorbidities of PolycysticOvarySyndromeAmong Indian Women. JAMANetwOpen. 024;7(10).

[7]. Ramanand SJ,GhonganeBB,RamanandJB,PatwardhanMH,Ghanghasrr,JainSS.Clinical characteristics of Polycystic Ovary Syndrome in Indian women.IJEM.2013Jan-Feb;17(1):138-145.

[8]. Kar S.Anthropometric, clinical, and metabolic comparisons of the four Rotterdam PCOS phenotypes: A prospective study of PCOS women.Journal of Human Reproductive Sciences .2013 Jul-Sep;6(3):194-200.

[9]. Cooney L G, Lee I, Mary,Sammel M D, Dokras A. High prevalence of moderate and severe depressive and anxiety symptoms in polycystic ovary syndrome: a systematic review and meta-analysis.Human Reproduction. May 2017;32(5): 1075–1091.

[10]. Kim JJ, Choi YM. Dyslipidemia in women with polycystic ovary syndrome. ObstetGynecol Sci. 2013 May;56(3):137-42.

[11]. Keeratibharat P, Sophonsritsuk A., Saipanish R. et al. Prevalence of depression and anxiety in women with polycystic ovary syndrome (PCOS) and associated factors in a quaternary hospital in Thailand: a crosssectionalstudy. BMCPsychiatry **24**,760(2024).

[12]. Marx TL, Mehta AE. Polycystic ovary syndrome: pathogenesis and treatment over the short and long term. Cleveland Clinic journal of medicine. 2003 Jan 1;70(1):31-45.

[13]. Esparza LA, Schafer D, Ho BS, Thackray VG, Kauffman AS. Hyperactive LH ,Pulses and Elevated Kisspeptin and NKB Gene Expression in the Arcuate Nucleus of a PCOS Mouse Model. Endocrinology.2020Apr1;161(4).

[14]. Wang K, Li Y, Chen Y. Androgen excess: a hallmark of polycystic ovary syndrome. Front Endocrinol (Lausanne).2023Dec 13;14:1273542. PMC10751361.

[15]. Sadeghi HM, Adeli I, Calina D, Docea AO, Mousavi T, Daniali M, et al.Polycystic Ovary Syndrome:A Comprehensive Review of Pathogenesis, Management, and Drug Repurposing. Int J Mol Sci. 2022 Jan 6;23(2):583.

[16]. Ndefo U A, Eaton A., Green M R., Polycystic Ovary Syndrome A Review of Treatment Options With a Focus on Pharmacological Approaches., P&T. June 2013;38: 336-355.

[17]. Chang S., Dunaif A., Diagnosis of Polycystic Ovary Syndrome: Which Criteria to Use When?:HHS Public Access; 2021., March; 50(1): 11–23.

[18]. Elisabeth M S, McLennan A, Rotterdam criteria, the end.Australasian Society for Ultrasound in Medicine.2018 May;21(2):59-60.

[19]. Sirman S M,Parish R C,et.al.Epidemiology and Comorbidities of Polycystic Ovary Syndrome in an Indigent Population.Journal of InvestigativeMedicine.2014;62(6) 868-874.

[20]. Palambo S, SantagniS.,et.al., Complications and challenges associated with polycystic ovary syndrome: current perspectives., International Journal of Women's Health.,2015;(7):745-763

[21]. Palomba S, Colombo C, Busnelli A, Caserta D, Vitale G. Polycystic ovary syndrome and thyroid disorder: a comprehensive narrative review of the literature. Front Endocrinol (Lausanne). 2023 Aug 11;14:1251866.

[22]. Megwalu UC, Moon PK. Thyroid cancer incidence and mortality trends in the United States: 2000-2018. Thyroid (2022) 32:560–70.

[23]. Pierpoint T, McKeigue PM, Isaacs AJ, Wild SH, Jacobs HS. Mortality of women with polycystic ovary syndrome at long-term follow-up. J Clin Epidemiol 1999; 51: 779-786.

[24]. Cho LW, Jayagopal V, Kilpatrick ES, Atkin SL. The biological variation of C-reactive protein in polycystic ovarian syndrome. Clin Chem 2005; 51: 1905-1907.

[25]. Legro RS, Kunselman AR, Dunaif A. Prevalence and predictors of dyslipidemia in women with polycystic ovary syndrome. Am J Med 2001; 111: 607-613.

[26]. Raikowha M, Glass MR, Rutherford AJ, Michelmore K, Balen AH. Polycystic ovary syndrome: a risk factor for cardiovascular disease Br J ObstetGynecol 2000; 107: 11-18
[27]. Giallauria F, Orio F, Palomba S, Lombardi G, Colao A, Vigorito C. Cardiovascular risk in women with polycystic ovary syndrome. J Cardiovasc Med 2008; 9: 987-992
[28]. Wild RA. Long term health consequences of PCOS. Hum Reprod Update 2002; 8: 231-241
[29]. Chapin JC, Hajjar KA. Fibrinolysis and the control of blood coagulation. Blood Rev. 2015 Jan;29(1):17-24.
[30]. Joshi A, Aluko A, Styer AK, Young BC, Johnson KM, Hacker MR, Modest AM. PCOS and the risk of pre-eclampsia. Reprod Biomed Online. 2022 Nov;45(5):961-969.
[31]. Daniilidis A, Dinas K. Long term health consequences of polycystic ovarian syndrome: a review analysis. Hippokratia. 2009 Apr;13(2):90-2
[32]. British Cardiac Society; British Hypertension Society; Diabetes UK; HEART UK; Primary Care Cardiovascular Society; Stroke Association. JBS 2: Joint British Societies' guidelines on prevention of cardiovascular disease in clinical practice. Heart. 2005 Dec;91 Suppl 5(Suppl5):v1-52.
[33]. Clinical green top guidelines. RCOG 2007: 33
[34]. Cheung AP. Ultrasound and menstrual history in predicting endometrial hyperplasia in polycystic ovary syndrome. ObstetGynecol 2001; 98: 325-331
[35]. Schmandt RE, Iglesias DA, Co NN, Lu KH. Understanding obesity and endometrial cancer risk: opportunities for prevention. AmJ Obstet Gynecol. 2011 Dec;205(6):518-25.
[36]. Johnson JE, Daley D, Tarta C, Stanciu PI. Risk of endometrial cancer in patients with polycystic ovarian syndrome: A meta-analysis. Oncol Lett. 2023 Mar 8;25(4):168.
[37]. Zeina Haoula, Maisa Salman, William Atiomo, Evaluating the association between endometrial cancer and polycystic ovary syndrome, Human Reproduction, Volume 27, Issue 5, May 2012, Pages 1327–1331
[38]. Brown J, Frumovitz M. Mucinous tumors of the ovary: current thoughts on diagnosis and management. Curr Oncol Rep. 2014 Jun;16(6):389.
[39]. Makieva S, Saunders PT, Norman JE. Androgens in pregnancy: roles in parturition. Hum Reprod Update. 2014 Jul-Aug;20(4):542-59.
[40]. Gottschau M, Kjaer S, Jensen A, Munk C, Mellenmkjaer L. Risk of cancer among women with polycystic ovary syndrome: a Danish cohort study. Gynecol Oncol. 2015;136:99–103
[41]. Harris HR, Terry KL. Polycystic ovary syndrome and risk of endometrial, ovarian, and breast cancer: a systematic review. Fertil Res Pract. 2016 Dec 5;2:14
[42]. Pillay OC, Te Fong LFW, Crow JC, Benjamin E, Mould T, Atiomo W, Menon PA, Leonard AJ, Hardiman P. The association between polycystic ovaries and endometrial cancer. Hum Reprod.2006;21:924–929.
[43]. Rossing MA, Daling JR, Weiss NS, Moore DE, Self SG. Ovarian Tumors in a Cohort of Infertile Women. N Engl J Med. 1994;331:771–776
[44]. Trabert B, Lamb EJ, Scoccia B, Moghissi KS, Westhoff CL, Niwa S, Brinton LA. Ovulation-inducing drugs and ovarian cancer risk: results from an extended follow-up of a large United States infertility cohort. Fertil Steril. 2013 Dec;100(6):1660-6.
[45]. Mishra GD, Pandeya N, Dobson AJ, Chung HF, Anderson D, Kuh D, Sandin S, Giles GG, Bruinsma F, Hayashi K, Lee JS, Mizunuma H, Cade JE, Burley V, Greenwood DC, Goodman A, Simonsen MK, Adami HO, Demakakos P, Weiderpass E. Early menarche, nulliparity and the risk for premature and early natural menopause. Hum Reprod. 2017 Mar 1;32(3):679-686
[46]. Richard S. Legro, Silva A. Arslanian, David A. Ehrmann, Kathleen M. Hoeger, M. Hassan Murad, Renato Pasquali, Corrine K. Welt, Diagnosis and Treatment of Polycystic Ovary Syndrome: An Endocrine Society Clinical Practice Guideline.The Journal of Clinical Endocrinology & Metabolism, Volume

98, Issue 12, 1 December 2013, Pages 4565–4592,

[47]. Atiomo W, El Mahdi E, Hardiman P. Familial associations in PCOS. Fertil Steril 2003; 80: 143-145

[48]. McCartney CR, Marshall JC. CLINICAL PRACTICE.Polycystic Ovary Syndrome. N Engl J Med 2016;375:54-64.

[49]. Rosenfield RL. Current concepts of polycystic ovary syndrome pathogenesis. Curr OpinPediatr2020;32:698-706.

[50]. Cooney LG, Dokras A. Depression and Anxiety in Polycystic Ovary Syndrome: Etiology and Treatment. Curr Psychiatry Rep 2017;19:83.

[51]. Zhao J, Fan J, Wang X. Study on the prevalence and clinical characteristics of polycystic ovary syndrome in female infertile patients. J PracGyneco Endocrino2019;6:137-8.

[52]. Cooper ID. Bibliometrics basics. J Med Libr Assoc2015;103:217-8.

[53]. Palomba S, Orio F Jr, Falbo A, Russo T, Tolino A, Zullo F. Effects of metformin and clomiphene citrate on ovarian vascularity in patients with polycystic ovary syndrome. Fertil Steril. 2006;86(6):1694–1701

[54]. Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and treatment of polycystic ovary syndrome: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2013;98(12):4565–4592

[55]. Selma Feldman Witchel, Sharon E Oberfield, Alexia S Peña, Polycystic Ovary Syndrome: Pathophysiology, Presentation, and Treatment With Emphasis on Adolescent Girls, Journal of the Endocrine Society, Volume 3, Issue 8, August 2019, Pages 1545–1573,

[56]. Abdalla MA, Deshmukh H, Atkin S, Sathyapalan T. A review of therapeutic options for managing the metabolic aspects of polycystic ovary syndrome. Ther Adv Endocrinol Metab. 2020 Jul 6;11.

[57]. Akre S, Sharma K, Chakole S, Wanjari MB. Recent Advances in the Management of Polycystic Ovary Syndrome: A Review Article. Cureus. 2022 Aug 4;14(8):e27689.

[58]. Rasquin LI, Anastasopoulou C, Mayrin JV. Polycystic ovarian disease. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. [Updated 2022 Nov 15].

[59]. Lim, S., Smith, C.A., Costello, M.F. et al. Barriers and facilitators to weight management in overweight and obese women living in Australia with PCOS: a qualitative study. BMC EndocrDisord **19**, 106 (2019).

[60]. Teede H, Deeks A, Moran L. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. BMC Med. 2010;8:41.

[61]. Szczuko M, Kikut J, Szczuko U, Szydłowska I, Nawrocka-Rutkowska J, Ziętek M, Verbanac D, Saso L. Nutrition Strategy and Life Style in Polycystic Ovary Syndrome-Narrative Review. Nutrients. 2021 Jul 18;13(7):2452.