



Global Trends And Management Of The Polycystic Ovarian Syndrome.

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ABSTRACT -

PCOS is the primary cause of infertility among women globally and is an endocrine condition associated with type II diabetes. In the social science literature, PCOS has not gotten much attention, even though it is regarded as a "lifestyle" disease. There is concern in India that an increasing number of urban middle-class Indian women are being affected by the illness, according to media reports citing eminent physicians. Doctors, the general public, and women who are affected by the syndrome all blame stress, altered lifestyles, modernity, "Westernization," and disturbed circadian cycles for the illness.

Since 1991, when neoliberal reforms were implemented and the nation became more exposed to globalization, these variables have been linked to shifts in diets, gender roles, and aspirations.

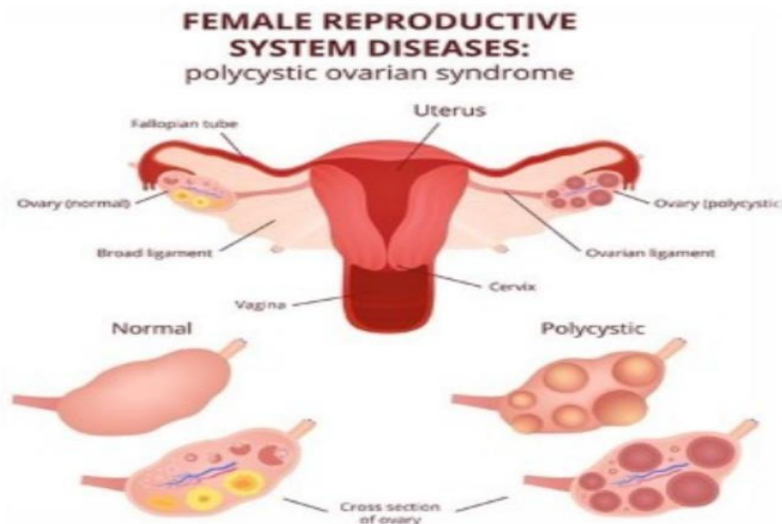
Women who have PCOS are now viewed as living examples of the biosocial stressors connected to contemporary urban middle-class living, and discussions on PCOS are used as a platform to express concerns about social, political, and economic changes in the nation. In this paper, we highlight the local understanding of PCOS as relating to an ecosocial viewpoint that underlines the structural vulnerabilities of urban middle-class women. The research is based on ethnographic fieldwork conducted in Mumbai, India, with 141 participants between 2012 and 2014.

While the majority of studies on structural vulnerabilities and health have focused on marginalized and economically deprived populations, we use PCOS as a case study to highlight the rise in lifestyle disorders associated with the effects of globalization and middle-class pressures to adopt "modern" identities and aspirations.

Keywords – Polycystic ovarian syndrome, Pathophysiology of PCOS, Etiology of PCOS, Global trends of PCOS, Management of PCOS

Introduction -

Polycystic Ovary Syndrome (PCOS), a common endocrine disorder that is the leading cause of female infertility worldwide. PCOS is characterized by multiple small ovarian follicles that resemble cysts, visible on sonograms, but none of them mature or ovulate, leading to irregular or absent menstrual cycles. The exact cause of PCOS is unknown, though genetic and lifestyle factors are thought to contribute. The syndrome has a range of symptoms, including cystic acne, male-pattern hair loss, hirsutism (excessive hair growth), insulin resistance, and dark patches of skin. Obesity is both a symptom and a contributing factor, worsening other symptoms. Insulin resistance is seen as a key factor in the development of PCOS, and some argue it is central to the syndrome's pathology. Additionally, the condition increases the risk of diabetes and cardiovascular disease. Treatment often focuses on weight loss and managing symptoms. Medications, such as hormonal contraceptives, ovulation inducers, and insulin sensitizers, are commonly used. The paper also notes that not all women with PCOS exhibit all symptoms, and the condition can present in "lean" women as well as those who are overweight. Finally, the paper emphasizes that while PCOS is often associated with ovarian dysfunction, it is a multisystem endocrine disorder that affects various parts of the body, and it may be related to metabolic abnormalities akin to those seen in men with similar symptoms, such as insulin resistance and hormonal imbalances.



PCOS Pathophysiology:

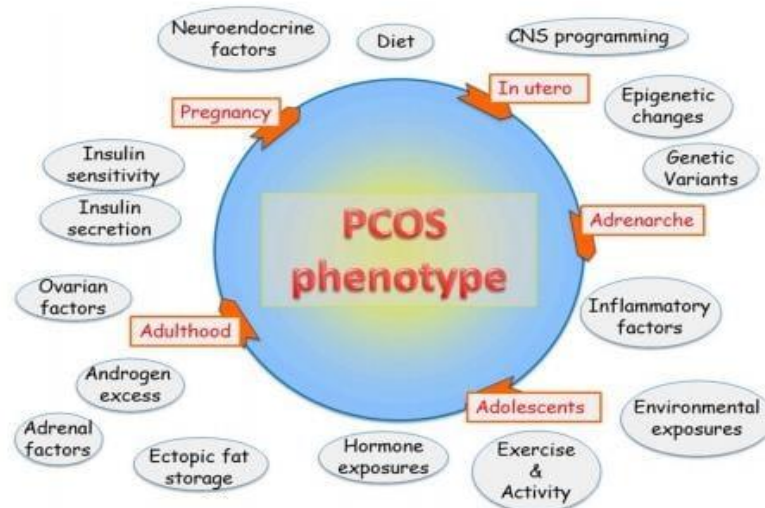
The complex and still poorly understood etiology of Polycystic Ovary Syndrome (PCOS), despite its high prevalence. The condition is thought to result from multiple interconnected pathophysiological pathways, which can vary among individuals. Historically, PCOS has been conceptualized as a "vicious cycle" that can start at various points within the reproductive system, ultimately leading to similar outcomes, such as anovulation (lack of ovulation) and excess ovarian androgens (male hormones). These hormonal imbalances contribute to key symptoms such as irregular menstrual cycles and excess hair growth (hirsutism). The paper highlights that the relationship between ovarian morphology (the appearance of cysts), hirsutism, menstrual disturbances, and obesity was first described by Stein and Leventhal in the 1930s. Their work demonstrated that ovarian wedge excision—removing part of the ovary—helped some women resume regular menstruation, pointing to ovarian dysfunction as a core contributor to PCOS.

Even though it is one of the most prevalent endocrinopathies, the etiology has not yet been fully explained. Although the definition of each contributory pathophysiological mechanism has been slow to emerge, the heterogeneity of PCOS may possibly reflect numerous pathophysiological causes. It has historically been helpful to think of polycystic ovarian syndrome as the outcome of a "vicious cycle," which might start at any one of numerous entry sites. Anovulation and excess ovarian androgen are the outcomes of altered function at any stage of the cycle.

The pathophysiology of PCOS has been explained by a number of theories:

- * A main neuroendocrine malfunction resulting in an enlarged LH pulse frequency and amplitude:
- * A distinct defect in insulin action and secretion that causes hyperinsulinemia and insulin resistance.
- * A flaw in androgen synthesis that causes the generation of more androgen by the ovaries. an increase in the production of androgens by the adrenal glands due to a change in the metabolism of cortisol.

However, it must be acknowledged that each of these is artificial, indicating that we have a good understanding of the intimate relationship between the metabolic, ovarian, and pituitary circuitry.



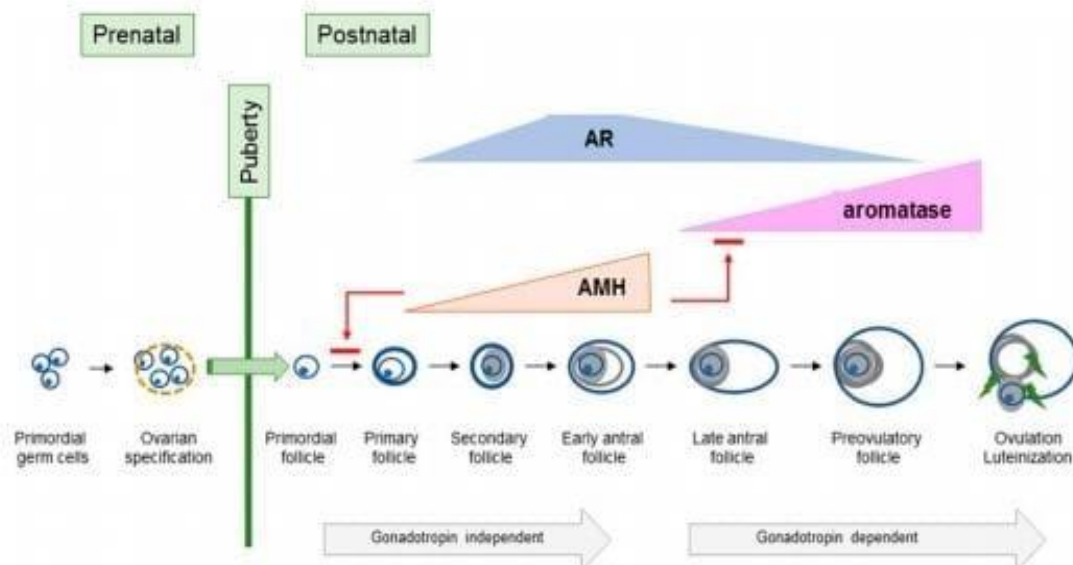
Several factors are involved in the clinical manifestations of PCOS, which explains why the syndrome can vary so widely among women. These factors include:

- **Insulin resistance:** Impaired sensitivity to insulin, which plays a central role in the metabolic aspect of PCOS.
- **Abnormal follicle-stimulating hormone (FSH) secretion:** Disruption in the regulation of this hormone, which is responsible for stimulating ovarian follicles to mature.
- **Hypersecretion of luteinizing hormone (LH):** Elevated levels of LH, which can disrupt the menstrual cycle and contribute to excess androgen production.
- **Excess testosterone:** Elevated male hormones that cause symptoms such as hirsutism and acne.

These interconnected factors contribute to the wide variation in how PCOS manifests clinically and why individualized approaches are needed in patient care.

1. Androgen excess:

Although not always present, the most persistent biochemical abnormality in PCOS is an increased level of testosterone and/or androstenedione in the serum. The majority of evidence points to the ovary as the primary source of hyperandrogenemia, though adrenal androgen excess may be present in a minority of patients. Evidence exists for an intrinsic abnormality of theca cell function, which may be the initiating pathology of PCOS.



2. Hypersecretion of LH (Luteinizing Hormone):

Women with PCOS often experience increased LH secretion, characterized by both higher frequency and amplitude of LH pulses. This leads to overstimulation of ovarian theca cells, which are responsible for producing androgens (male hormones like testosterone). This increase in androgens contributes to many of the symptoms of PCOS, such as hirsutism and acne. Evidence suggests that this altered LH secretion may be driven by androgen excess itself. Normally, progesterone provides a negative feedback on LH secretion, but in PCOS, this feedback is impaired. However, androgen receptor blockers can help restore

3. Abnormal FSH (Follicle-Stimulating Hormone) Secretion:

FSH levels in women with PCOS are typically within the normal range but are lower than expected during the early follicular phase compared to women with regular menstrual cycles. This is thought to be due to abnormal ovarian steroid production, particularly from inactive but steroidogenic antral follicles (follicles that haven't fully matured). These follicles still produce some steroids, which improperly suppress FSH secretion. As a result, suboptimal FSH levels fail to promote normal follicular growth, leading to an ovulation (lack of ovulation) and irregular or absent menstrual cycles.

4. Insulin Resistance:

Insulin resistance is common among women with PCOS, although not all affected women exhibit it. Obesity exacerbates insulin resistance, and it tends to be more pronounced in women with PCOS compared to those with normal ovarian function. Interestingly, central adiposity (fat accumulation around the abdomen) appears to be a more significant predictor of insulin resistance than overall obesity. Even lean women with PCOS, who may have a higher proportion of abdominal fat compared to women without PCOS, are more likely to experience insulin resistance. This highlights the importance of abdominal fat as a key factor in the metabolic disturbances associated with PCOS.

5. Hypertension -

Arterial hypertension (AH) is defined by the World Health Organization as a systolic blood pressure (SBP) > 140 mmHg and diastolic blood pressure (DBP) > 90 mmHg, or the use of antihypertensive drugs. A study in North East Brazil found that women with polycystic ovary syndrome (PCOS) had a 2-fold higher prevalence of AH compared to those without PCOS (18.6% vs. 9.9%, $P < 0.05$). Insulin resistance (IR) and hyperinsulinemia contribute to AH in PCOS by affecting vascular smooth muscle, impairing vasodilation, and activating the renin-angiotensin-aldosterone system. Additionally, high testosterone levels and low sex hormone-binding globulin (SHBG) increase the risk of elevated SBP and DBP, with a significant odds ratio (OR: 3.817, $P = 0.029$).

Etiology -

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder with a multifactorial cause, involving genetic, environmental, and hormonal factors. Polycystic ovary syndrome (PCOS) is influenced by both genetic and environmental factors. Unhealthy lifestyles, poor diet, and infections can increase the risk. Insulin resistance raises insulin levels, disrupting ovarian function and increasing androgen levels, which causes anovulation. Hormonal imbalances, including altered levels of gonadotropin-releasing hormone, FSH, LH, and prolactin, are also common. Genetic factors play a significant role, with 241 gene variations linked to PCOS, including mutations in genes related to androgen receptors, LH, FSH, and leptin. These genetic changes disrupt ovarian function and biochemical pathways. Polymorphisms in genes like StAR, FSHR, FTO, and others are associated with PCOS. Increased insulin and androgen levels worsen PCOS, affecting ovarian cells and promoting fat accumulation, which contributes to insulin resistance.

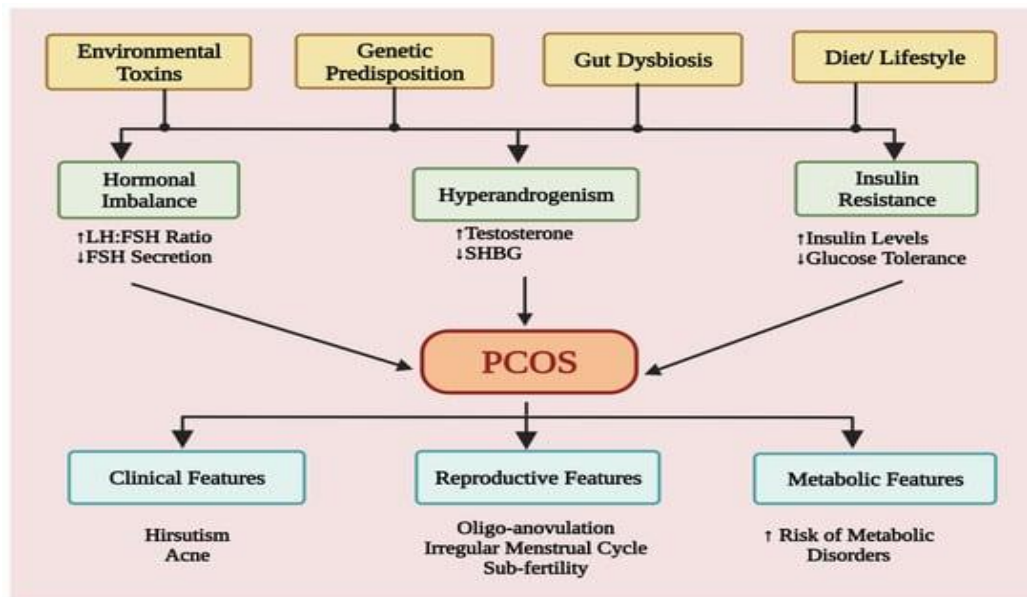
Key contributors include:

1. Hereditary Factors: PCOS tends to run in families, especially among mothers and sisters, suggesting a genetic predisposition.

2. Genetic Variants: Specific genetic variations linked to insulin regulation, hormone production, and inflammation have been identified.

3. Hormonal Imbalance: Elevated androgen levels (male hormones like testosterone) are common, leading to symptoms such as excessive hair growth, acne, and male-pattern baldness.

4. Insulin Resistance: Many women with PCOS experience insulin resistance, where cells fail to respond effectively to insulin, potentially leading to higher insulin levels in the body.



Global Trends in PCOS -

Polycystic Ovary Syndrome (PCOS) is influenced by various risk factors, though its exact cause remains unclear. These factors include:

1. Genetics: A family history of PCOS increases the likelihood of developing the condition, particularly if a close female relative, like a mother or sister, has it.

2. Insulin Resistance: Many women with PCOS have insulin resistance, where the body's cells don't respond properly to insulin, leading to higher insulin levels. This can increase androgen production and disrupt ovulation.

3. Obesity: Excess weight can worsen insulin resistance and exacerbate PCOS symptoms, though the condition can also affect women of normal weight.

4. Inflammation: Women with PCOS often experience low-grade inflammation, which may further increase androgen levels and worsen symptoms.

5. Hormonal Imbalances: Elevated levels of luteinizing hormone (LH) are commonly seen in PCOS, contributing to the hormonal imbalance that characterizes the disorder.

2. Education and Awareness:

The global awareness of PCOS has grown dramatically over the last decade. Social media campaigns, educational programs, and advocacy by healthcare organizations have all played important roles in raising awareness about this disorder. September has been designated as PCOS Awareness Month, with several programs aimed at educating the public and healthcare professionals about early identification and treatment techniques.

Management -

Handling metabolic concomitant conditions: other treatment options

Lifestyle modifications –

Over half of PCOS patients are overweight or obese, and weight management is a key part of treatment. A combination of a healthy, balanced diet and regular exercise can help improve metabolism, increase insulin sensitivity, and support safe weight loss. While exercise is important, diet plays a crucial role in managing PCOS symptoms. Indian women, in particular, may not prioritize diet, but a high-fiber, high-protein diet (about 1 gram of protein per kilogram of body weight) is recommended. A 30% calorie deficit, or 500 to 750 kcal/day, is typically advised (around 1200 to 1500 kcal/day).

Research shows that losing as little as 5% of body weight can restore normal menstrual cycles, improve ovulation, and enhance the effectiveness of fertility treatments, leading to better pregnancy outcomes.

Genetics:

Genetic variations are believed to contribute to PCOS, as supported by a meta-analysis of genome-wide association studies (GWAS). These variations may affect different mechanisms related to PCOS, including traits like obesity and insulin resistance (IR), which could impact treatment options like combination oral contraceptive pills (OCPs).

Ovulation Inducers:

Ovulation induction is a key treatment for women with PCOS who are struggling with infertility, as about 70% of these women experience anovulation (lack of ovulation). Ovulation inducers are crucial for helping these women conceive. The first-line treatment for triggering ovulation in adolescents with PCOS is clomiphene citrate (CC), a selective estrogen receptor modulator (SERM). It works as an anti-estrogen by blocking estrogen receptors in the hypothalamus, which increases gonadotropin-releasing hormone (GnRH) and follicle-stimulating hormone (FSH) production. This process helps stimulate follicle growth. Typically, CC is prescribed for five days, starting on the second day of the menstrual cycle, with an initial dose of 50 mg, which can gradually be increased to 150 mg per day. For women who are resistant to CC, it can be combined with metformin to improve outcomes, based on moderate-quality evidence. About 30% of pregnancies in women using CC result in a successful pregnancy, but 20% of these pregnancies may end in miscarriage or stillbirth. Common side effects of CC include ovarian enlargement, ovarian hyperstimulation syndrome, multiple pregnancies, hot flashes, bloating, and fatigue.

Aromatase inhibitors (AI)—letrozole –

Aromatase converts androgens into estrogens. In the third generation, letrozole is the most often used non-steroidal selective AI for ovulation induction. Letrozole prevents ovarian estradiol release. When the pituitary gland secretes more FSH, the follicles become more sensitive to the hormone, increasing the rate of ovulation. This is due to the hypothalamus's release of negative feedback and a brief increase in androgens in the ovary.

Gonadotropins –

Gonadotropin therapy for women with anovulatory PCOS. Patients who have failed first-line oral ovulation stimulation drugs might explore this as a second-line option, such as AI and SERM.

Insulin sensitizing agents –

In PCOS, insulin secretion and function are disrupted, leading to hyperinsulinemia and insulin resistance. High insulin levels can affect ovarian function, causing increased androgen production, which interferes with follicular development and leads to the polycystic ovarian appearance characteristic of PCOS. Acanthosis nigricans, a skin condition, is often used as an indicator of insulin resistance. Insulin resistance not only exacerbates PCOS symptoms but also increases the risk of long-term health issues, such as type 2 diabetes and cardiovascular disease, both of which are serious and potentially fatal. Therefore, managing insulin resistance through medications and lifestyle changes is essential in treating PCOS and preventing these long-term complications.

Metformin -

Metformin is a commonly used insulin sensitizer for treating PCOS and is also approved for managing type 2 diabetes. It works by improving insulin sensitivity in peripheral tissues, reducing hepatic glucose production, increasing glucose uptake, and inhibiting glucose synthesis in the liver. While metformin is generally safe and effective, it can cause side effects such as nausea, vomiting, diarrhea, and abdominal discomfort. Women with PCOS are at an increased risk of developing pre-diabetes or type 2 diabetes (T2DM), particularly when obesity is present, which can complicate the diagnosis and treatment. Metformin has been shown to help reduce the risk of developing T2DM in these women. Additionally, PCOS patients often have a poorer lipid profile, with lower HDL cholesterol and higher triglyceride levels, increasing their risk of cardiovascular issues. Managing dyslipidemia is therefore a critical aspect of PCOS treatment. However, because some women experience intolerance to metformin and its side effects, alternative treatments should be considered for those who cannot tolerate the medication.

Inositol –

Inositol Supplemental inositol helps with insulin signaling. Its function in controlling the metabolic and biochemical aspects of PCOS is poorly understood. A recent study suggests that ovulation and menstrual cycles may be enhanced. Inositol has little benefits, which is why this suggestion advises against using it, but it is also inexpensive and has a minimal risk of side effects.

Glucagon-like peptide-1 receptor analogue –

Proteinogenesis that increases glucose-dependent insulin release, particularly after a meal, include glucagon-like peptide 1 (GLP1) and glucose-dependent unguided polypeptides (GIP). This phenomenon is known as potentiation. Response to the incretins A shift in the function of incretin is associated with insulin resistance, particularly in type 2 diabetes. According to a recent study, PCOS individuals had decreased levels of incretin. Because of the enhanced

glycemic control and weight loss in type 2 diabetes patients, focusing on this system as a therapeutic option has become a viable option. A promising medication called mimetics targets a particular metabolic target and can be used to treat PCOS in a variety of patients.

Statins –

Dyslipidemia, characterized by low HDL-C, high triglycerides, and high LDL-C, is a significant risk factor for cardiovascular disease in women with PCOS. Effective treatment for PCOS may involve improving lipid profiles to reduce cardiovascular risk. The class of drugs known as statins, which block cholesterol production (e.g., atorvastatin, rosuvastatin, simvastatin), have shown promise in managing PCOS. Statins block the enzyme HMG-CoA reductase, reducing cholesterol synthesis and lowering oxidative stress, as indicated by decreased serum malondialdehyde (MDA) levels in obese women with PCOS. Atorvastatin has also been shown to lower levels of DHEAS and androstenedione and improve vitamin D status in PCOS patients. However, statins should not be used in fertile women due to their teratogenic risks, and further research is needed to confirm their long-term effectiveness in PCOS treatment.

Antiandrogens –

Antigens such as finasteride, Spiro lactone, and flutamide help PCOS patients with their acne and hirsutism. These antigens may be helpful for those with elevated lipid levels, which are common in PCOS patients. The effects of 100 mg of spironolactone, 250 mg of flutamide, and 5 mg of finasteride were studied in 40 hirsute women over a period of six months. All three medications worked, even though there were no notable differences between the groups. Due to its affordability, accessibility, and safety, spironolactone (25– 100 mg twice daily) is the antiandrogen that is most frequently administered.

Oral Contraceptives (OCs) –

These are commonly used to treat PCOS by regulating menstruation and reducing symptoms like hirsutism (excessive hair growth), acne, and other androgenic effects. Combination OCs containing both estrogen and progestogen are particularly effective in lowering testosterone levels, thus addressing these symptoms. Over time, many women see clinical improvement in hirsutism after about six months of OC therapy. These medications may also work synergistically with anti-androgen treatments to enhance results.

Medroxyprogesterone acetate (MPA)-

It is another treatment used in PCOS, especially for women with irregular uterine bleeding or amenorrhea (absence of menstruation). It is also used in women who are not seeking pregnancy. MPA helps regulate the menstrual cycle, reduces ovarian androgen production, and has a positive impact on lipid profiles and insulin sensitivity, though it has little effect on abnormal endometrial growth.

Discussion –

To far, numerous research have looked into the prevalence of PCOS in women. As far as we are aware, no meta-analysis has evaluated the prevalence of PCOS worldwide. Therefore, the goal of the current systematic investigation was to evaluate the prevalence of PCOS worldwide. Following the systematic review, 35 cross-sectional studies were analyzed based on inclusion and exclusion criteria. Our findings revealed that the global prevalence of PCOS was 5.5% (95% CI:3.9-7.7%) using NIH criteria, 11.5% (95% CI: 6.6- 19.4%) using Rotterdam criteria, and 7.1% (95% CI: 2.3-20.2%) using AES criteria. A self- report subgroup study revealed that the prevalence of PCOS was 11% (95% confidence interval: 5.2-21.8%). Given the substantial heterogeneity observed by the research, which can be caused by the diverse sample sizes, different years of publication, the race of the examined women, the age of the investigated women, as well as different diagnostic criteria, meta-regression test, and subgroup analysis utilized to investigate the factors impacting the heterogeneity. This demonstrates that these factors were effective in creating heterogeneity, because the results of meta-regression show that as women's ages and sample sizes increase in different studies, the prevalence decreases, while the prevalence increases as the studies become more up to date. Furthermore, the subgroup analysis varies by region, and differing prevalence's may be reported across continents dependent on race. This study found a higher prevalence caused by the diverse sample sizes, different years of publication, the race of the examined women, the age of the investigated women, as well as different diagnostic criteria, meta-regression test, and subgroup analysis utilized to investigate the factors impacting the heterogeneity.

Conclusion –

Polycystic Ovary Syndrome (PCOS) is a common hormonal disorder affecting women of reproductive age, characterized by polycystic ovaries, excess androgen, and irregular menstrual cycles. The condition is associated with various metabolic issues, including obesity, insulin resistance, and an increased risk of type 2 diabetes and cardiovascular disease. While there is no cure for PCOS, it can be effectively managed with a combination of pharmacological treatments (such as hormone therapy and metformin for insulin resistance) and lifestyle changes (including diet and exercise). Proper management can help women lead healthy lives and reduce the risk of long-term complications. PCOS also requires a comprehensive treatment approach, with early diagnosis and personalized care being crucial for symptom relief and overall health. In the context of infertility, lifestyle changes should be the first line of treatment, before considering medication. Studies suggest that PCOS may increase the risk of endometrial cancer, although it does not appear to affect the risk of ovarian or breast cancer. These findings highlight the potential increased risk of gynecological cancers in women with PCOS, underscoring the importance of regular monitoring and tailored care.

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10. International Journal of Trend in Scientific Research and Development (IJTSRD) Volume: 3 | Issue: 4 | May-Jun 2019 Available Online: www.ijtsrd.com e-ISSN: 2456 - 6470 @ IJTSRD | Unique Paper ID - IJTSRD23542 | Volume – 3 | Issue – 4 | May-Jun 2019 Page: 60 A Review on “Polycystic Ovary Syndrome (PCOS)” Miss Dipamoni Morang1, Pankaj Chasta2, Mr. Kaushal K. Chandrul3