A Review of Polycystic Ovarian Syndrome

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Abstract- *PCOS is a prevalent female endocrine gynaecology condition that affects 6-15% of reproductive age women. It is a complicated disorder characterised by high androgen levels, irregular menstruation, and/or tiny cysts on both ovaries. PCOS patients hormonal abnormalities and metabolic difficulties, which can affect their general health and appearance. Androgen excess and insulin resistance are now thought to be responsible for a large portion of the phenotypic manifestation. However insulin resistance is far from ubiquitous. It is distinguished by irregular menstruation, acne, and is linked to type 2 diabetes and cardiovascular disease. Efficient PCOS management opens the door to avoiding the danger of related problems. Hyperandrogenism, a clinical hallmark of PCOS, can cause follicular development inhibition, micro cysts in the ovaries, an ovulation, and menstrual abnormalities, as well as type 2 diabetes and cardiovascular disease. The treatment aims to address (IR), the consequences of Hyperandrogenism, irregular menstruation, and infertility. This article focuses on the genesis, pathophysiology, diagnosis and therapy of polycystic ovarian syndrome.*

Keywords- Polycystic ovary syndrome, Hyperandrogenism, Hirsutism, Phenotypic manifestation, insulin resistance,

I. INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a prevalent female endocrine condition that affects 6-15% of the female population (1). It is distinguished largely by a very ovulation does not occur due to an irregular menstrual cycle (2). The hypothalamus is a significant endocrine gland that is implicated with PCOS. Pituitary gland, ovaries, adrenal gland, and peripheral adipose tissues that contributes to an overall imbalance. Insulin resistance is frequent in PCOS (3) and has been linked to both metabolic and reproductive issues (4).

Although the high ratio of luteinizing hormone (LH) to follicle stimulating hormone (FSH) and increased frequency of Gonadotropin-releasing hormone (GnRH) are recognized to be an fundamental causes of PCOS (5,6), the specific etiology and pathophysiology are not fully understood. Evidence shows that several external and internal variables, including as insulin resistance (IR), Hyperandrogenism (HA), environmental factors, genetics, and epigenetic, all have a role. Further more, PCOS raises the risk of subsequent consequences such as cardiovascular disease (6,7) type-2 diabetes mellitus metabolic syndrome depression, and anxiety (8). Hirsutism, irregular menstruation, persistent an ovulation, and infertility are typical clinical characteristics. Chronic Hyperandrogenism is linked to defective hypothalamic-pituitary feedback, LH hyper secretion, premature granulosa cell luteinization, abnormal oocyte maturation, and premature arrest of activated Primary follicles (9).The most important step in managing this illness is to drop at least 5% of body weight; hence, frequent exercise and fat and sugar-free meals are also suggested to every lady suffering with PCOS. The specific origin and pathophysiology of PCOS are unknown (10). Ultrasound, magnetic resonance imaging (MRI), and computed tomography scanning (CT) are routinely used to detect PCOS (11).

II. ETIOLOGY

PCOS is an oligogenic condition in which the combination of several genetic and environmental variables determines the diverse, clinical, and biochemical phenotype (12). Although the genetic aetiology of PCOS is unknown, a family history of PCOS is rather prevalent; nevertheless, familial ties to PCOS are unclear. A formal segregation study is impossible due to a lack of phenotypic data. Nonetheless, current research reveals that PCOS clustering in families reflects an autosomal dominant pattern (13). Environmental variables associated with PCOS (e.g., obesity) can be aggravated by poor food choices and physical inactivity; infectious agents and chemicals may also play a role . PCOS's reproductive and metabolic characteristics are potentially reversible with lifestyle changes such as weight loss and exercise (14). PCOS is an oligogenic condition in which the combination of several genetic and environmental variables determines the diverse, clinical, and biochemical phenotype (12). Although the genetic aetiology of PCOS is unknown, a family history of PCOS is rather prevalent; nevertheless, familial ties to PCOS are unclear. A formal segregation study is impossible due to a lack of phenotypic data. Nonetheless, current research reveals that PCOS clustering in families reflects an autosomal dominant pattern (13). Environmental variables associated with PCOS (e.g., obesity) can be

aggravated by poor food choices and physical inactivity; infectious agents and chemicals may also play a role (13). PCOS's reproductive and metabolic characteristics are potentially reversible with lifestyle changes such as weight loss and exercise. (14)

III. PATHOPHYSIOLOGY

The pathophysiology of PCOS involves primary defects in the hypothalamic-pituitary axis, insulin secretion and action, and ovarian function (15,16). Although the cause of PCOS is unknown, PCOS has been linked to insulin resistance and obesity. The association with insulin function is expected; insulin helps to regulate ovarian function, and the ovaries respond to excess insulin by producing androgens, which can lead to an ovulation.(15) Follicular maturation arrest is a hallmark sign that an ovarian abnormality exists.

PCOS is characterised by elevated luteinizing hormone (LH) and gonadotropin-releasing hormone (GnRH) levels, while follicular-stimulating hormone (FSH) levels are low or unchanged. As GnRH levels rise, the ovarian thecal cells produce more androgens. (17). Follicular arrest can be treated by increasing endogenous FSH levels or by administering exogenous FSH (16).

According to some studies, PCOS is a primary defect in young girls entering puberty who have a family history of the disorder. Prolactin levels are elevated in about 25% of PCOS patients (18).Obesity is a common comorbidity of PCOS, but it is not required for diagnosis.

IV. RISK FACTORS

A. EXTRNAL FACTORS
B. INTERNAL FACTORS

A.EXTERNAL FACTORS :

a) Physical and emotional stress :

Psychological disorders are frequently the cause of PCOS. Increased stress can disrupt the normal menstrual cycle and cause hormonal changes such as increased cortisol and prolactin levels, which affect menstruation normally resumes once the stress has passed (19). The hypothalamic-pituitary-adrenal (HPA) axis releases cortisol in response to stress (20,21). Cortisol promotes IR by increasing visceral fat accumulation, gluconeogenesis, and lipolysis (21) Furthermore, cortisol stimulates glucose production in the liver (21). Stress is also a factor involved in insulin enhancement (20). Other stress influences on PCOS include anti-mullerian hormone (AMH) inference and changing sex hormone levels (20, 21).

b) Diet:

Although the role of nutrition in PCOS is unclear, studies have found a link between certain nutrient levels and PCOS indices. Saturated fatty acid (SFA) consumption contributes to PCOS by causing inflammation status (22), as well as decreasing insulin sensitivity (23). Taking SFAs causes inflammation by increasing TNF- levels in the blood and expressing a s suppressor Vitamin D deficiency may aggravate PCOS or the comorbidities caused by PCOS (24). Calcitriol increases the mRNA and protein levels of insulin receptors. It also directly and indirectly increases insulin sensitivity. The direct effect is achieved by activating PPAR-, a receptor involved in fatty acid metabolism in adipose tissue and skeletal muscle. The indirect impact is on intracellular calcium regulation, which is critical for insulin-mediated signalling in fat and muscle. Vitamin D deficiency, on the other hand, may cause insulin resistance by inducing an inflammatory response (25). Furthermore, Vitamin D inhibits the AMH promoter.

Several hypotheses have been advanced to explain the pathogenesis of PCOS:

- Endometrial progesterone resistance.
- An abnormality in insulin secretion and action.
- A flaw in androgen synthesis that leads to increased ovarian androgen production.
- A change in cortisol metabolism that leads to increased adrenal androgen production (26).

c) Endometrial progesterone resistance:

In women, endometrial responsiveness to progesterone is reduced. with PCOS, and a study found that total endometrial progesterone Women with PCOS have higher receptor expression. Increased Progesterone receptor expression in epithelial cells is higher than in other cells. That in PCOS women's stromal cells, implying a lower Progesterone binding in stromal cells (27). Disorders that begin in childhood indicate a genetic component pubertal For up to 2 years, the onset may be temporary. The onset after marriage denotes Obesity and stress. And onset away from the physiological point indicates a tumour Sclerocystic ovaries appear 6-18 months after a pelvic infection (28).

B) INTERNAL FACTORS:

a) Insulin resistance:

Insulin resistance (IR) affects 60-80% of the population. Women with PCOS and is partially independent of body weight (29). Insulin resistance and compensatory hyperinsulinemia have an impact on both. PCOS metabolic and reproductive aspects (30). Insulin resistanceis recognised as a major metabolic pathophysiologic mechanism disturbances, endothelial dysfunction, and atherosclerosis (31).

Increased testosterone production leads to abnormal ovulation. Hyperinsulinemia is most likely caused by both increased insulin secretion and decreased insulin clearance. Anovulatory women with PCOS are more insulin resistant and hyperinsulinaemic than ovulatory women with PCOS (32). The aetiology of PCOS is heavily reliant on selective insulin resistance. As a result, compensatory hyperinsulinaemia may result in a lower level of serum hormone binding globulin (SHBG), act as a trophic stimulus to androgen production in the adrenals and ovaries, and have a direct effect on the hypothalamus, causing abnormally stimulated appetite and increased gonadotropin secretion. It includes peripherally reduced insulin receptor activity, which leads to PCOS endocrine dysfunction. (33). Obesity increases insulin resistance and hyperinsulinaemia (34). Insulin stimulates ovarian and adrenal androgen production and may affect gonadotropin secretion. It is also responsible for decreased SHBG synthesis in the liver increasing the level of free testosterone in the blood Insulin for ovaries. One of the causes is thought to be hyperinsulinemia. the mechanisms that drive ovarian androgen production Bodymass index, hyperandrogenaemia, and clinical Hyperandrogenism are independent predictors of insulin resistance (35). Modified steroid LH negative feedback regulation, in conjunction with compensatory. Hyperinsulinemia caused by insulin resistance can interfere with ovulatory function leading to an ovulation (36). PCOS has been linked to pancreatic beta-cell secretary dysfunction as well as insulin resistance. The cell defect increased insulin secretion at rest but decreased it after meal. (37)

Insulin‘s two major action contribute to Hyperandrogenism in PCOS:

- Serum sex hormone binding globulin synthesis is inhibited in the liver (SHBG).
- Inhibition of hepatic IGFBP-1 production, allowing for increased IGF-1 levels and greater local activity (38).

Overall, hyperandrogenism and insulin resistance are intertwined in the pathogenesis of reproductive and metabolic diseases.

b) Hyperandrogenism:

The increased production of ovarian androgens is the cause the syndrome's main source of androgen excess. In turn, androgen Excessive amounts have both intraovarian paracrine and neuroendocrine effects (39) Effects on the hypothalamic-pituitary axis (40),contributing to an ovulation. In general, hyperandrogenism (HA) lowers SHBG (sex hormone binding globulin) levels, resulting in higher levels of free testosterone (41). PCOS women have higher levels of testosterone in their blood, which can be converted to estrone in adipose tissue. Increased estrone to estradiol conversion affects follicle growth and raises the LH/FSH ratio, resulting in ovulatory dysfunction (42).

HA can cause an increase in AMH (anti-mullerian hormone), which inhibits ovulation and follicle development via a different mechanism. Androgen excess promotes the development of preantral follicles in the ovary. as well as small antral follicles from their primordial and primary follicle (43) stages The presence of an increased number of small antral follicles in the comparison to the normal ovary, the polycystic ovary producesincreased Anti-mullerian hormone (AMH) concentrations (44), a hormone produced by preantral and antral granulosa cells. Antral follicles are small. The greater the total amount of circulating AMH in PCOS may result from more than just an increase in small follicles pool, as well as increased AMH secretion per follicle (45). Increased AMH may, in turn, counteract the actions of FSH. Despite contributing to an ovulation (46), Although hyperandrogenism is a major factor in the development of PCOS, it is not the only factor.

c) Increased peripheral cortisol metabolism:

Increased androgen production was discovered in 25% of PCOS women as a result of a genetic trait or as a result of ovarian hormonal secretion. This involves the irreversible inactivation of 5 reductase and 5 reductase in the liver, as well as the reversible interconversion of 11HSD with cortisol in the liver and adipose tissue (47)

The main effect of insulin on the ovaries is not only increased androgen production but also disruption of androgen synthesis regulation, preventing down-regulation .LH receptors, resulting in increased androgen production and oestrone, which, when combined with the insulin effect, lowers SHBG. Hyperestrogenism and decreased FSH levels (48). Hyperinsulinemia may also suppress hepatic sex hormone production binding globulin (SHBG), which increases androgenicity (49).There will be an imbalance between FSH and LH in PCOS women. When the ovary is

stimulated to produce an egg, it ripens but does not rupture .Instead, it begins to build in the ovaries. . As LH levels rise, the egg may begin to grow and remain as a cyst in the ovary, preventing occultation. Unruptured follicles produce testosterone (50, 51). PCOS is frequently characterised by insulin resistance and hyperinsulinemia, and the majority of patients in clinical series are overweight or obese. These factors are important in the pathogenesis of androgen excess and the susceptibility to develop glucose intolerance states and type 2 diabetes (T2DM) earlier than expected.(52, 53).

d) Obesity:

Obesity also contributes to the development of hyperinsulinemia, IR, and HA. Non-esterified fatty acids (NEFAs) levels in the blood rise with visceral obesity. Instead of glucose, skeletal muscles use NEFAs as an energy source. This hyperglycemia results into hyper insulinemia and a rapid pancreatic reaction (55). Furthermore, the lipolytic response of visceral fat to catecholamines causes lipotoxicity (44) as well as insulin clearance and activity impairment (54).

V. MANAGEMENT

The management strategy and the best therapy option are determined by the target patient and her priorities (55). Complications can range from seeking fertility to regulating menstrual irregularities to weight loss or relief from hyperandrogenic symptoms such as acne, hirsutism, or androgenic alopecia (56). To achieve the best results, the approach should be suited to each individual (77). There is no single ideal treatment for all women diagnosed with PCOS, leaving doctors with no choice but to use symptomatic therapy (58).

LIFESTYLE MODIFICATION AND NON-PHARMACOLOGICAL APPROACHES:

1. Weight loss

Weight gain in women with PCOS is caused by elevated androgenic hormone levels, particularly in the abdominal area. As a result, many PCOS women have an apple-shaped body rather than a pear-shaped body (62). Weight loss and calorie restriction would be the first steps for women diagnosed with PCOS (60). Many studies show that even a 5% to 10% weight loss can restore a regular menstrual cycle (61). It would be preferable for obese women to achieve their normal BMI range (BMI). Along with weight loss, free testosterone levels fall, and the prevalence of metabolic syndrome falls (56).

2. Diet

As previously stated, the best diet or nutrient regimen for each woman would be suited (61). However, some suggestions may help you decide whether to eat more or less. A healthy diet would be high in fibre and low in saturated fats and carbohydrates. There are two types of carbohydrates based on their blood glucose response within two hours: low and high glycemic index carbohydrates. Low glycemic index carbohydrates are at the top of our list; these include foods and vegetables such as broccoli, raw carrot, lentils, soy, bran breakfast cereals, whole-grain bread, and so on. Patients should also be aware of foods with a high glycemic index for prevention, such as white rice, cakes and cookies, fries or chips, and some fruits such as pineapple or watermelon (62).

3. Exercise

Exercise and physical activity are essential for weight loss. They may help to improve insulin sensitivity (63). Different studies recommend different times for exercise during the week, but the American Heart Association (AHA) recommends 150 minutes of moderate exercise or 75 minutes of vigorous and intense exercise per week (56). Several studies show that exercise, with or without a diet, can help women with PCOS resume ovulation. Exercise may influence ovulation by modulating the hypothalamic-pituitary-gonadal (HPG) axis. Exercise lowers insulin and free androgen levels in overweight and obese women, restoring HPA ovulation regulation (63).

COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM)

Current PCOS management and medications are only moderately effective, and some cases remain untreated despite non-pharmacological and pharmacological treatments. According to some studies, pharmacologically based therapies are only effective in 60% of patients (66). Recent research has shown that using complementary and alternative medicine (CAM) as an adjunctive therapy may benefit management (64). Today, complementary and alternative medicine (CAM) is a well-known approach that has been used at some point in the lives of more than 70% of PCOS patients. According to the latest edition of the National Center for Complementary and Integrative Health (NCCIH), complementary approaches can be classified into three classes based on their primary therapeutic input: nutritional, psychological, physical, or all of them in combination. One of the significant benefits of complementary and alternative medicine is that people often accept these methods because of their beliefs and cultures, which leads to better adherence or tolerance to the therapy. According to previous research, various CAM methods such as traditional Chinese medicine (TCM), immunotherapy, diet

therapy (herbal and medicinal foods, probiotics, and vitamin or supplementation therapy), psychotherapy, spa, yoga, Tai Chi, and oxygen therapy are effective in reducing the severity of PCOS and its complications (64). The following sections discuss two critical subgroups of CAM that are effective in PCOS management.

1. Acupuncture

Acupuncture, a key component of complementary and alternative medicine, has been used in China for over 3000 years (64). It is a type of sensory stimulation in which thin needles are inserted into the skin and muscles. Acupuncture improves clinical manifestations of PCOS by activating somatic afferent nerves of the skin and muscles, modulating somatic and autonomic nervous system activity, and endocrine/metabolic functions (65). Endorphin production increases during acupuncture, influencing gonadotropin-releasing hormone secretion, ovulation, and the menstrual cycle. This means that acupuncture may induce ovulation and restore the menstrual cycle (66).

2. Supplementations

Aside from FDA-approved medications, numerous supplementation products have been shown to be effective in some women with PCOS. Vitamin D supplements, resveratrol, α-lipoic acid, omega-3, berberine, folic acid, myoinositol (MI), and d-chiro-inositol are among the products available (DCI).

Several studies have shown that vitamin D is effective, especially during the colder months of the year. Because vitamin B12 deficiency is thought to play a role in the pathogenesis of PCOS, only the compensatory amount is recommended (67).

Resveratrol is one of the most commonly prescribed supplements for the treatment of PCOS. It is thought to have chemopreventive, anti-inflammatory and antioxidant properties, as well as cardioprotective and neuroprotective properties (67). Resveratrol, like statins, may be beneficial in PCOS by inhibiting HMG-CoA reductase expression and activity (69). This product has been shown in clinical trials to reduce IR and the risk of developing type 2 diabetes .

The anti-inflammatory and antioxidant properties of alpha-lipoic acid and omega-3 fatty acids have been shown to improve women's lipid profiles and insulin sensitivity (55).

Berberine is a nutraceutical compound that may have beneficial effects on IR and obesity, particularly visceral adipose tissue (VAT) (78). Folic acid is commonly prescribed to PCOS women seeking fertility .

Finally, MI and DCI are important and well-studied supplements for PCOS treatment. MI has been shown to improve insulin receptor activity and potentially restore ovulatory function in the majority of PCOS women (58). Inositol has an effect on intracellular metabolic processes by activating key enzymes that control the oxidative and non oxidative metabolism of glucose. Studies on PCOS women who took MI alone, DCI alone, or these combinations of the two found that they caused increased ovulation frequency, decreased need for FSH therapy to trigger ovulation, and a significant improvement in pregnancy rate (68).

PHARMACOLOGICAL TREATMENTS

Before pursuing pharmacological approaches, all women diagnosed with PCOS, regardless of weight, complaint, or anything else, must be given healthy lifestyle advice. This is because, in the majority of cases, especially in mild to moderate forms, women can benefit solely from diet and exercise . However, the treatment would be primarily determined by the patient's choices and the condition of others. If the patient does not want to become pregnant and primarily complains about irregular menstruation, combined oral contraceptives (COCs) or progestins are the drugs of choice. The physician can select the best oral contraceptive based on other symptoms rather than menstrual irregularity; for example, Yasmin®, Yaz®, or other agents can have antiandrogenic effects and, as a result, reduce androgen production. As a result, they may be beneficial to those suffering from hirsutism and/or acne complications.

Metformin, a biguanide, is typically prescribed in combination with first-choice drugs (COCs) to restore the ovulation cycle in PCOS women due to its insulin sensitivity-increasing properties. Metformin also has antihyperandrogenic properties in the short term.

Agents such as aldosterone receptor antagonists (e.g., spironolactone) and 5-alpha reductases (e.g., finasteride) would be more beneficial in other patients who simply want relief from dermatological manifestations of hyperandrogenism. For those with infertility who require ovulation induction drugs such as clomiphene citrate and/or aromatase inhibitors, treatment options change (84).

Of course, there are many limitations and precautions, and not everyone can benefit from the above-mentioned agents due to adverse effects or contraindications. Many COC agents cause nausea and vomiting by attempting to stimulate the body's pregnancy situation. Furthermore,

those who take them frequently experience depression, headaches, and migraines. Metformin also causes nausea and vomiting in the first few days of use, which may not be tolerated by all patients and leads to therapy discontinuation.
Spironolactone, a commonly used and prescribed agent for androgen-related complications, has the potential to cause hyperkalemia. As a result, it is advised to look up the adverse reactions or contraindications in reliable drug literature or to make enquiries about the patient's history of any possible reaction prior to writing the prescription.

DRUG REPURPOSING IN PCOS

Drug repurposing, also known as drug repositioning or drug re-tasking, is the process of discovering new indications for a medication that has previously been on the market and has USFDA approval for a specific therapeutic goal (73). Given that the medicines have passed pre-clinical and clinical, safety, and immunological tests, using this method has shortened the duration of the research and development process. As previously stated in this review, PCOS still lacks a single ideal pharmacological treatment, and doctors typically treat patients' symptoms with other agents. Examining other drugs, mostly diabetes medications, may help identify some new medications for women with PCOS-related complications.

1. Citrate of clomiphene:

In PCOS patients, it is used as the first-line treatment for ovulation induction. The oestrogen receptor antagonist is the culprit. Negative feedback of the oestrogen signalling pathway results in increased FSH availability. Follicular growth is induced by increased FSH (55). It includes the first part of the menstrual cycle (75). It is also used in the treatment of infertility.

2. Metformin:

Insulin sensitizing agents such as metformin, troglitazone, are antagonize some hyperandrogenic signs, by reducing total and free testosterone concentration (79). It increases ovulation and reduces the problem caused by insulin resistance and regulates excessively raised levels of androgens.2 It restores menstrual cycle, ovulation and fertility(80). Short term treatment of 3-6 mo of metformin in PCOS to improve ovulatory functions and circulating androgen is fall (82). During pregnancy, it reduces number of pregnancy related problem such asgestational diabetes and gestational hypertension (84).

3. Flutamide:

It proposed as alternative to spironolactone, which act by inhibiting the androgen receptor.3 It is the non-steroidal pure antiandrogen which inhibit the androgen receptor in a dose dependent manner and not having better efficacy than spironolactone .

4. Glucocorticoids:

Prednisone and dexamethasone have been used to induce ovulation .In PCOS patients with high adrenal androgen, low dose dexamethasone (0.25-0.5 mg) at bed time can be used (81).

5. Gonadotropins:

It is used as second line of therapy after resistance to clomiphenecitrate. It induces ovulation, maintain and provoke optimum follicle growth with the controlled administration of FSH4 and its treatment started with low doses (82).

6. N-acetyl-cysteine (NAC):

It has antioxidant required for the body’s production of glutathione which inhibit the oxidative stress and prevention of hyperinsulinaemia (87).

VI. DIAGNOSIS

Polycystic ovary syndrome is difficult to diagnose due to the intrinsic characteristics of the syndrome: the heterogeneity of the symptoms; their variability in different age ranges1. PCOS is difficult or impossible to diagnose in adolescent and menopausal women because the puberty mimics the signs and symptoms of polycysticovary syndrome. Menarche is also the appearance of multiple small antral follicles, and it is very easy to confuse. In menopausal women, the recall of menses is highly inaccurate and also on the basis of biochemical hyperandrogenaemia (86).

- **Recent diagnostic parameters**

Anti-mullerian hormone [AMH] levels proposed as a parameter toreplace ultra-sonographic assessment. Another diagnostic parameter is an assessment of ovarian stromal volume, measured as a ratio of stromal area to the total area of the ovary (S/A ratio) .A physical examination is measuring blood pressure, weight and height should be completed. A routine and general physical examination should also have conducted and note the presence of secondary sex characteristics, along with palpation of thyroid gland for masses or enlargement.

- **Differential diagnosis [5]**

The clinician must consider several possibilities including:

- Exogenous androgens.
- Androgen secreting tumours.
- Acromegaly.
- Cushing's syndrome.
- Primary ovarian failure.
- Thyroid dysfunction.
- Diagnostic evaluation and work-up.
- Routine physical examination.
- BMI->30 is obese.
- BP recording.
- Laboratory investigations.
- Demonstration of biochemical Hyperandrogenaemia.
- S: estradiol and FSH estimations.
- Laparoscopy.(83)
- Hysteroscopy.
- **Oestrone** : -Serum androgen concentrations have little attention in diagnosis (85).
- **Vitamin D :** -Deficiency of vitamin D is common in women with PCOS. Especially in obese ones. Its deficiency also affect fertility in women with PCOS (85).

VII. CONCLUSION

PCOS is common endocrine disorder in premenopausal women. It is characterized by irregular menstrual cycle, acne and also associated with type-2 diabetes mellitus and cardiovascular disease. The fundamental defect of PCOS remain unknown. Lifestyle modification along with pharmacological therapies that improve hyperandrogenism and improve insulin sensitivity, assisting regular menstrual cycle and increased fertility and preventing cardiovascular and other consequences.

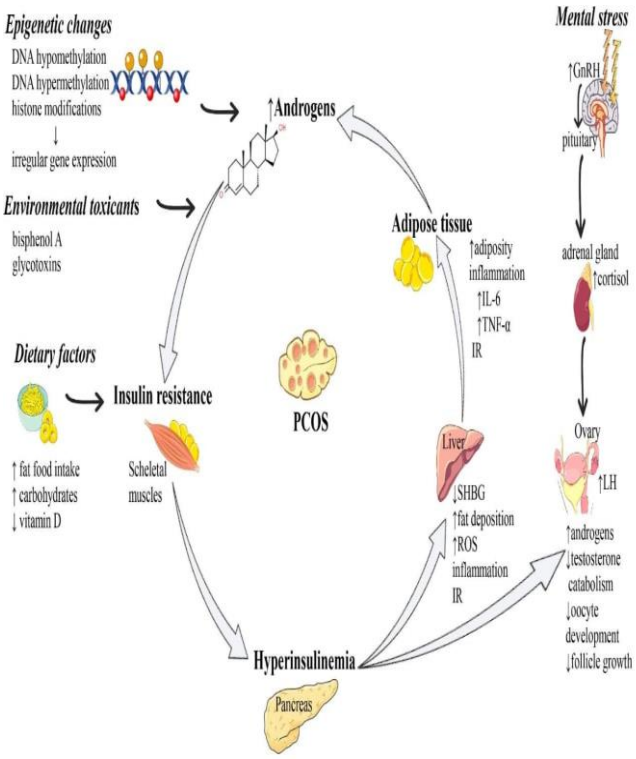

FIGURE 1 SUMMARIZED SCHEME OF REGARDING TO PATHOPHYSIOLOGY OF PCOS

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