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Impact of Polycystic Ovary Syndrome on the General and Reproductive Health of Women

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Abstract
Polycystic ovarian syndrome (PCOS) is a female endocrine condition that many women who are reproductive age experience. despite a piece of the mechanism contributory in appearance of PCOS has been find out,the precise etiology and pathogenesis aren't well known. The extrinsic and intrinsic factors responsible for PCOS have been evaluated. Studies show a higher risk of type 2 diabetes and high blood pressure, and dyslipidemia, that this translate into an elevated risk of cardiovascular events irrespective of weight, according to current evidence. psychical health issues, Anxiety and despair are prevalent side effects that do not get enough attention, as do fatty liver disease not related to alcohol and endometrial cancer. Doubts remain about if these hazards are present in all PCOS patients or whether are they limited to certain types. and whether the risks persist after menopause. Additionally, more research is required to discover whether focused interventions and systematic screening might produce better results. Clinicians who treat women with PCOS must advice patients about long-term health concerns and develop techniques to limit illness progression and cause chronic diseases that impair women's general health until such evidence is accessible.

Keywords: Polycystic Ovary Syndrome (PCOS), External Factors, Internal Factors, Women Health, Reproductive

Introduction

PCOS could be one of many causes of the prevalent conditions in women, and providing healthcare for women is still challenging., often transferring patients from one doctor to another in an attempt to understand their disorder, Women often go through long periods before diagnosis, in which they see several doctors before a confirmed diagnosis, this syndrome combines many medical specialties to improve the care of women with this syndrome, As this type of medical problem combines many specialties between obstetrics, gynecology, pediatrics, endocrinology, internal medicine, genetics, psychology and laboratory medicine, all

of them work on the scientific conception of polycystic ovarian syndrome and the diagnosis of all its aspects, When just the expenses of initial diagnosis and reproductive endocrinology are taken into account, the financial cost of PCOS was originally anticipated to reach over $3.7 billion annually in 2020. (Carrie et al ., 2022).

PCOS is a widespread and complicated endocrine condition that has both short-term and long-term repercussions and impacts 5-20% of reproductive-age women. (Jia, 2018), while Akanksha et al. (2022) report that The most prevalent endocrine condition in women is PCOS. Females of childbearing age and the main cause of poor ovulation, which affects 3-13% of women, In addition to having an elevated danger of pregnancy-related issues gestational diabetes included and premature delivery, women with this syndrome also have variable degrees of metabolic, endocrine, and mental abnormalities (Tiantian et al., 2022).

PCOS affects numerous facets of health and well-being throughout the lifespan due to its influence on reproduction, metabolism, and mental health. It is the primary contributor to anovulation, obesity, type 2 diabetes, metabolic disorder, consuming disorders, anxiety, and depression, in addition to cardiovascular risk factors including elevated blood pressure. (Ismayilova & Yaya, 2022).

PCOS Description

PCOS is one of the most common hormonal illnesses in women between the ages of 15 and 45, and affects post-menopausal and reproductive health in 4–18% of women globally. (Hanan et al ., 2020). This syndrome is linked with ovarian enlargement and dysfunction in terms of increased androgen level, insulin resistance, etc. (Witche et al., 2019) and is distinguished by the appearance of tiny cysts containing ovarian fluid (Dunaif & Thamas, 2001).

Despite the fact that elevated “luteinizing Hormone (LH)” to “Follicle-Stimulating Hormone (FSH)” ratios and rise gonadotropin (GnRH) production are recognized to be the most important underlying causes of PCOS (Bednarska & Siejka,2017), the causes and exact diseases were not comprehensively known as well. (Bednarska & Siejka,2017; Ganie et al ., 2019). Evidence supports the presence of both external and endogenous variables, including insulin resistance (IR), hyperandrogenism (HA), and genetic factors. Furthermore, it should be noted PCOS raises the chance of further issues such as cardiovascular disease , Type 2 diabetes (Ganie et al ., 2019; Glueck & Goldenberg,2019) metabolic syndrome, depression, and anxiety (Damone et al ., 2019).

Diagnosis

PCOS is one of the disorders that can̓t be identified using standard diagnostic methods such as blood testing, culture, and biopsy; As a result, PCOS can̓t be accurately diagnosed using a test.. The discriminatory diagnosis except for related disorders is called according to the symptoms and narrows the options. To determine the differential analysis of “PCOS, Hyperprolactinemia, Thyroid Disease, Cushing's Syndrome, and Adrenal Hyperplasia”, it must be eliminated based on the available data (Witchel et al ., 2019). Although a medical history, weight fluctuations, and insulin resistance symptoms may be useful in retrospect, a pelvic exam, transvaginal ultrasound, and hormone measurement are among the most commonly recommended

examinations. (Polycystic Ovary Syndrome (PCOS),2021).[1] In addition, The Rotterdam parameters are the most extensively used technique for diagnosing PCOS in adults. Ultrasound, To determine the diagnosis of PCOS, factors such as ovulatory failure, polycystic ovaries, or clinical or biochemical hyperandrogenism would all be considered. (European Society of Human Reproduction and Embryology,2018).

Pathophysiology of PCOS

One of the most constant biochemical aspects of PCOS is androgen secretion. Anomalies in the hypothalamic-pituitary-gonad axis at all levels are the root cause of this. LH regulates androgen production from cholesterol in ovarian cells, whereas FSH regulates granulocyte aromatase activity, It governs the amount of estrogen generated from androgenic precursors When LH is higher than FSH, the ovaries preferentially create androgens. (that is when LH-FSH is elevated). The percentage of LH and FSH produced by the pituitary gland is determined by the frequency of GnRH pulses in the hypothalamus. LH b subunit transcription is encouraged over FSH subunit transcription by the raise frequency of hypothalamic GnRH pulses. which raises the LH/FSH ratio and stimulates the synthesis of androgens It has been proposed that women with PCOS have a larger percentage of LH-FSH. Their GnRH pulse frequency has increased. (Dumesic et al ., 2020).

Insulin resistance is involved in the development of hyperandrogenism in both direct and indirect ways, complicating its role in PCOSInsulin and LH cooperate in the ovary to stimulate androgen synthesis by theca cells. Additionally, insulin prevents the liver's output of sex hormone-binding globulin (SHBG), which raise the quantity of unbound (free) or physiologically active testosterone in the blood and improves the effect of circulating androgens. Less apparent reasons of ovulatory failure include, but it is believed to be caused by excessive androgenThe polycystic ovarian type is distinguished by a marked inability select the main follicle and a cluster of antral follicles about 2 to 8 mm in size. This look is hypothesized to be caused by an androgen-induced halt in antral follicle growth. (Dumesic et al ., 2020).

Symptoms of PCOS

Polycystic ovary syndrome is accompanied by several symptoms, including infertility, menstrual cycle disorder, oligomenorrhea,which is defined as a period of no menstruation lasting more than month, or amenorrhea, which is known as a period of no menstrual flow lasting more than 90 days., which is an indicator of lack or absence of ovulation and is related to low fertility(Decherney & Nathan , 2006) , Hirsutism, acne, insulin resistance, obesity, elevated level of insulin-like evolution factor 1 (IGF-1), presence of ovarian cysts, milk production, Acnthosis nigricans (which are black spots that appear in the neck and armpits), depression (Cortet-Rudelli & Dewailly, 2006; Barnard et al ., 2007).

Etiology and Risk Factors

External Factors

Epigenetic Mechanism

Epigenetics point at to hereditary changes in genome and gene expression that do not involve changes in DNA sequence. (Ilie & Georgescu,2015; Casadesús & Noyer-Weidner,2013).

These modifications entail append or removing chemical components from DNA or histone (Mukherjee et al ., 2018). Women with PCOS have maximum LH activity.. It might be related to follicular growth and HA issues that are frequent in PCOS patients. (Ibanez et al ., 2017). In theca cells, the LH/choriogonadotropin receptor (LHCGR) is in control of steroidogenesis. (Fenichel et al ., 2017). This receptor hypomethylation increases gene expression and LH sensitivity. (Ibanez et al ., 2017; Abbott et al ., 2019). The relationship between LHCGR overexpression and hypomethylated areas has been demonstrated in study on PCOS patients. (Ilie & Georgescu,2015; Fenichel et al ., 2017) on the surface of theca cells (Fenichel et al ., 2017). Furthermore, epoxide hydrolase 1 (EPHX1) is an energetic enzyme in the degradation of aromatic chemicals. (Ilie & Georgescu,2015; Fenichel et al ., 2017; Rutkowska & Diamanti-Kandarakis, 2016). Its gene promoter hypomethylation (Ilie & Georgescu,2015; Fenichel et al ., 2017) increases enzyme expression. EPHX1 overproduction lowers testosterone to estradiol conversion, may lead to PCOS. (Ilie & Georgescu,2015). Moreover.

The function of the ovaries is influenced by peroxisome proliferator-activated receptor gamma (PPAR-). (Ilie & Georgescu,2015; Ibanez et al ., 2017; Fenichel et al ., 2017; Qu et al ., 2012). PPAR hypermethylation, nuclear co-repressor 1 hypomethylation (Fenichel et al ., 2017; Qu et al ., 2012), and change in histone deacetylase 3's acetylation, both of which are PPAR co-repressors. (Ilie & Georgescu,2015), seen in PCOS individuals that have HA (Ilie & Georgescu,2015; Fenichel et al ., 2017; Qu et al ., 2012). These changes were discovered in the granulosa cells of PCOS women. (Ibanez et al ., 2017; Li et al ., 2019).

Environmental Toxicants

Endocrine-disrupting chemicals are explane by the ‘United States Environmental Safeguard Agency (USEPA)”. (EDC) in human body, as horonal synthysis, secretion, then transport and binding action interferes within; it is clear that they are responsible for behavior such maintenance and reproduction also development (Rocha et al ., 2019). When EDCs attach to hormone receptors, they can either bind as agonists or antagonists. (Jones & Regan, 2019) EDCs are practically everywhere we go in our daily lives. They resemble the actions of steroid hormones because their structures are composed of phenols or halogens such as chlorine and bromine (Rutkowska & Diamanti-Kandarakis, 2016). Studies have confirmed that women with PCOS had a maximum serum content of EDCs (Rutkowska & Diamanti-Kandarakis, 2016; Merkin et al ., 2016). PCOS susceptibility may result from prolonged and ongoing exposure to EDCs from prenatal through puberty (Rutkowska & Diamanti-Kandarakis, 2016; Calina et al ., 2019).

As an epitome, consider bisphenol A. (BPA) BPA is a man-made chemical that is found in polycarbonate plastics and epoxy resins. (Jones & Regan, 2019; Sobolewski & Barrett, 2014), Dental fillings, food and beverage packaging (Jones & Regan, 2019), baby bottles, and polyvinyl chloride are all examples of polyvinyl chloride (PVC) (Sobolewski & Barrett, 2014), which influences metabolism via many routes BPA directly influences oogenesis. (Soave et al ., 2020) through interactio with estrogen receptor (ER) and the non-classical membrane ER, such as the G-protein coupled receptor 30 (GPCR30) (Rutkowska & Diamanti-Kandarakis, 2016; Sobolewski & Barrett, 2014; Soave et al ., 2020). Additionally, it increases androgen

release while preventing the breakdown of testosterone in theca cells (Rutkowska & Diamanti-Kandarakis, 2016; Soave et al ., 2020).

Another consequence of BPA on interstitial theca cells is androgen overproduction caused by 17-hydroxylase dysregulation (P450c17) (Sobolewski & Barrett, 2014; Palioura & Diamanti-Kandarakis,2015), P450scc (cholesterol side-chain cleavage enzyme) and steroidogenic acute regulatory protein (Palioura & Diamanti-Kandarakis,2015). In granulosa cells, BPA prevents the aromatase enzyme from being expressed and prevents the production of estrogen. Finally, it disrupts the intrafollicular environment, impairing oocyte growth and maturation. (Rutkowska & Diamanti-Kandarakis, 2016; Soave et al ., 2020). The indirect action of BPA on HA includes the downregulation of testosterone 2a-hydroxylase and testosterone 6b-hydroxylase enzymes in the liver, resulting in a greater testosterone concentricity. (Palioura & Diamanti-Kandarakis,2015; Palioura & Diamanti-Kandarakis,2013).

Furthermore, BPA acts as a potent replacement for testosterone by attaching to the sex hormone-binding globulin (SHBG), raising the concentricity of free testosterone. BPA and testosterone interact in a reciprocal manner; excess androgen reduces the liver's ability to excrete BPA by inhibiting the enzyme uridine diphosphate-glucuronosyl transferase. The amount of free BPA in the blood is elevated as a result of this process, exacerbating its harmful effects on the ovaries. (Rutkowska & Diamanti-Kandarakis, 2016; Soave et al ., 2020; Palioura & Diamanti-Kandarakis,2013).

Furthermore, it is thought that BPA may serve as an obesogen. (Sobolewski & Barrett, 2014; Palioura & Diamanti-Kandarakis,2015). It has an obesogenic effect by upregulating adipogenesis-related genes. (; Palioura & Diamanti-Kandarakis,2015), Adipocyte differentiation stimulation (Sobolewski & Barrett, 2014; Palioura & Diamanti-Kandarakis,2015), Potentiation of lipid accumulation in cells integrated in the medical syndrome, as well as activation of target cell transformation via the phosphatidylinositol 3-kinase pathway to adipocytes (Palioura & Diamanti-Kandarakis,2015). The stimulation of the glucocorticoid receptor causes adipogenesis in response to BPA. The enzyme responsible for converting cortisone to cortisol is made more active by the receptor's activation, which encourages adipogenesis (Sobolewski & Barrett, 2014; Palioura & Diamanti-Kandarakis,2015; Palioura & Diamanti-Kandarakis,2013).

Furthermore, BPA stimulates interleukin-6 (IL-6) and tumor necrosis factor (TNF) release (TNF-α) (Palioura & Diamanti-Kandarakis,2015; Palioura & Diamanti-Kandarakis,2013), both involving adiposity and IR (Palioura & Diamanti-Kandarakis,2015). Furthermore, it inhibits adiponectin release. (Sobolewski & Barrett, 2014; Palioura & Diamanti-Kandarakis,2013) as well as the helpful component for IR protection (Sobolewski & Barrett, 2014). It can also alter glucose homeostasis by impacting pancreatic cells directly.

In long-term exposure, BPA induces a persistent rise in insulin and additional IR. (Palioura & Diamanti-Kandarakis,2015) through influencing -pancreatic cells' mitochondrial activity and metabolic processes BPA inhibits glucagon production by suppressing the intracellular calcium ion fluctuation pattern in the absence of glucose. Another chemical category that affects bodily health in progress glycation final products (AGEs), commonly known as glycotoxins. AGEs are compounds that cause inflammation. (Wang et al ., 2019) that induce pro-inflammatory

pathways and oxidative stress by interacting with their RAGE (receptor for AGE) surface receptor (Soave et al ., 2020; Wang et al ., 2019). Exogenous AGEs can be ingested or created in the body by nonenzymatic glycation and oxidation of proteins and lipids(Rutkowska & Diamanti-Kandarakis, 2016).

Patients with PCOS have been observed to have increased serum AGE concentrations (Rutkowska & Diamanti-Kandarakis, 2016). AGEs inhibit pre-ovulatory follicle development via the ERK1/MAPK pathway and follicles damages through oxidative mediated by interaction of RAGE. This connection raises the level of inflammatory chemicals within the cell. Glycotoxins are likely to promote adipogenesis, according to in vitro experiments on 3T3-L1 cell lines. (Rutkowska & Diamanti-Kandarakis, 2016). A greater BMI, on the other hand, coincide to a reduced level of RAGEs soluble that are glycotoxin clearance responsible for and AGE deposition in the reproductive system, particularly in the ovaries. (Rutkowska & Diamanti-Kandarakis, 2016; Soave et al ., 2020).

In PCOS, this bidirectional relationship affects inflammatory processes and metabolic syndrome. (Rutkowska & Diamanti-Kandarakis, 2016). AGEs also play a role in IR ovaries (Rutkowska & Diamanti-Kandarakis, 2016; Soave et al ., 2020). In earlier studies, these chemicals impaired and transport glucose in the human KGN granulosa cell line and adipocytes decreased glucose absorption (Rutkowska & Diamanti-Kandarakis, 2016; Soave et al ., 2020). By inducing oxidative stress, inflammation, and protein glycation, all of which significantly reduce sensitivity of insulin, they also include IR. Furthermore, An arise in AGE levels alteration the insulin signaling system and coincide with glucose transporter activity 4 (GLUT-4) translocation. (Li et al ., 2019).

Physical and Emotional Stress

Despite the paucity of research on the effects of stress in PCOS, it is well recognized that the condition has a detrimental effect on mental and emotional well-being. Adipocyte hyperplasia and proliferation are induced by persistent stress. This happens as a result of how glucocorticoids affect the maturation of pre-adipocytes. Adipokine synthesis, Attraction of adipokines and stimulation of stromal fat immune cells are also connected to chronic stress. (Stefanaki et al ., 2018). Furthermore, By raising cytokines levels like IL-6 and TNF-, it is in charge of triggering an inflammatory state as well as upsetting the oxidant-antioxidant balance (Stefanaki et al ., 2018).

Furthermore, persistent stress is important in IR. In reaction to stress, the hypothalamic-pituitary-adrenal (HPA) axis secretes cortisol (Steegers-Theunissen et al ., 2020; Yang et al ., 2018). Cortisol promotes IR by increasing visceral fat storage, gluconeogenesis, and lipolysis. (Yang et al ., 2018). Furthermore, cortisol stimulates glucose synthesis in the liver(Yang et al ., 2018). Stress also has a role in increasing insulin levels(Steegers-Theunissen et al ., 2020). Other stress impacts on PCOS may include anti-mullerian hormone (AMH) inference and modifying cortisol sex hormone levels. (Steegers-Theunissen et al ., 2020; Yang et al ., 2018).

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Diet

Although it is unknown whether diet has an impact on PCOS, studies have discovered a bind between specific nutrient levels and PCOS pointers. Inflammation caused by saturated fatty acid (SFA) assimilation leads to PCOS (Szczuko et al ., 2021) as well as decreasing insulin sensitivity (Faghfoori et al .,2017). By boosting TNF- levels in the blood and expressing a specific cytokine suppressor, taking SFAs induces inflammation. (Szczuko et al ., 2021). A lack of vitamin D may aggravate PCOS(Faghfoori et al .,2017; Muscogiuri et al ., 2017) or the comorbidities brought on by PCOS (Muscogiuri et al ., 2017).

Calcitriol regulates the mRNA and protein levels of insulin receptors. additionally increases insulin sensitivity both directly and indirectly. By activating PPAR-, a receptor implicated in skeletal muscle and adipose tissue fatty acid metabolism, the direct effect is accomplished. The indirect effect is on intracellular Ca^{+} homeostasis, which is necessary for insulin-mediated signaling in adipose tissue and muscle (Muscogiuri et al ., 2017). other side, a lack of vitamin D may cause insulin resistance by inducing an inflammatory response. In addition, vitamin D blocks the AMH promoter (Ciebiera et al ., 2021).

Internal Factors

Insulin resistance, impaired glucose (IGT) & Type 2 diabetes.

PCOS is currently considered a metabolic condition marked by impaired insulin sensibility, as well as changes in insulin- specified insulin receptors and post-receptor cellular activity(Day et al ., 2015; Unluhizarc et al ., 2021). Insulin resistance and hyperinsulinemia change gonadotropin secretion, enhance ovarian androgen production and reduce sex hormone-binding globulin levels, all of which contribute to the syndrome's metabolic and reproductive difficulties (leading in elevated amounts of free androgen).

On the other side, androgens in PCOS may harm metabolism. New research suggests the importance of anabolic steroids, especially 11-oxygenated C19 steroids generated from the adrenal gland, which account for a significant amount of the total blood androgen aggregation in PCOS women and are carefully linked to insulin resistance indices (O'Reilly et al ., 2017). Aldo-keto reductase type 1C3 (AKR1C3) was found to be an essential driver of lipogenesis and insulin resistance in both in vivo and ex vivo experiments, suggesting a possible novel therapeutic target. Another prominent cause of increased androgen in PCOS is adipose tissue (O'Reilly et al ., 2017). Euglycemic-hyperinsulinaemic clamp trials, showed (27%) of insulin reduction sensitivity in PCOS patients (Cassa et al ., 2016).

Although a greater BMI accelerated this reduction and did so more than controls, this was independent of BMI. According to clamp studies, Women with the "classic" or "complete" phenotype experience more severe insulin resistance than do those with normoandrogenic or ovulatory phenotypes., suggesting that the subphenotype of PCOS may increase the chance of insulin resistance (Moghett et al ., 2013), Despite the modest impact of diagnostic criteria (Rotterdam vs. NIH) (Cassa et al ., 2016).

Consistent with the data of the studies, meta-analyses certain an augmentation danger of IGT and type 2 diabetes and PCOS young patients comparison to healthy women. Although this may be affected by race (5.2-, 4.4- and 2.6-fold for Asians, North/South Americans, and

Europeans, respectively) and body weight (4.4- and 2.5-fold for lean-matched and overweight/obesity-matched groups, respectively). In Asia and the Americas, women with PCOS had a 4.4- and 4.7-fold greater risk of type 2 diabetes, respectively.

In women with normal glucose tolerance, A higher incidence of dysglycemia or type 2 diabetes was associated with a family history of the condition, as well as unfavorable metabolic features (Ehrmann et al ., 2005). This was illustrated by the pilot study in which EHR data of more than 50,000 British women with PCOS were analyzed. We discovered an adjusted risk ratio of 1.75.52 for type 2 diabetes mellitus, with risk rising across all BMI categories. Weight gain, however, was a significant predictor of progression to a new diabetes diagnosis, with a 1% rise in BMI resulting in a 2% increase in risk. According to these observations, genetically elevated testosterone is detrimental to a woman's metabolism. Menopause (Cooney & Dokras, 2018) This risk is present in both lean and overweight/obese women, emphasizing the significance of check for type 2 diabetes in long-term care.

Obesity

There has been a lot of research done on how obesity affects female fertility. Obese women seem to have less reproductive potential.. Obesity has been associated to reduced ovulation, patchy menstruation, higher miscarriage rates, poor implantation, and pregnancy rates in women. (Brewer & Balen, 2010). Further, because central/abdominal obesity is connected with insulin resistance and has a bigger influence on fecundity, body fat distribution is crucial.

The central allocation of body fat that PCOS women are more prone to have is linked to high levels of androgens and insulin resistance (Dumesic et al ., 2020). In addition to having an impact on the disease's biochemistry and metabolism, obesity is a risk factor for PCOS that can exacerbate the consequences of insulin resistance (Wojciechowski et al. 2012). Adipose tissue is now an important source of energy storage and endocrine tissue.

It has also been demonstrated to have a vital role including reproduction, the process of immune system, metabolism of glucose and lipid, by secreting a group of bioactive cytokines known as adipokines. Adipokines are non-specific cytokines that are exclusive to adipose tissue or are produced first by adipocytes, such as adiponectin, resistin, tumor necrosis factor, and leptin (Chen et al, 2019).

Insulin Resistance (IR) and type 2 diabetes can cause abnormally high adipokine levels. PCOS individuals have an adipose tissue dysfunction, involves overproduction of pro-inflammatory adipokines such tumor necrosis factor-alpha and inadequate expression of "adipokines. Other 'beneficial' chemicals include adiponectin (Bohler et al. 2010; Chen et al, 2019). In a project conducted by Taha et al. 2022 on femel with PCOS, the results showed elevated levels of leptin, resistin, phosphatin, omentin, interleukin one beta (IL1β), tumor necrosis factor-alpha (TNFα), and triiodothyronine (T3). Thyroid-stimulating hormone (TSH, insulin, blood sugar, and body mass index (BMI).

PCOS phenotypic expression

The PCOS Rotterdam criteria included at least 2 of 3 characteristics: Oligo-Anovulation, PCOM, and Clinical or biochemical hyperandrogenism.whereas other endocrine diseases are

excluded. (Teede et al., 2018). The Rotterdam norm result in several kinds of PCOS, included classic PCOS for example, hyperandrogenism with anovulation with or without PCOS, polycystic ovaries (hyperandrogenic and PCOM), and non-androgenic PCOS(Ovulation and PCOM).

Another alteration is that the Association for the Study of Androgen Excess and PCOS (AE-PCOS) regards hyperandrogenism as a necessary component of PCOS. PCOS is classified as hyperandrogenism along with ovarian dysfunction (either anovulation and/or PCOS), except other disorders associated with androgen excess. Thus, the prevalence of PCOS doubled by 6-10 percent by 1990 using NIH criteria using the broader Rotterdam riteria, with PCOS defined by the 1990 NIH being the most common phenotype (Rotterdam, 2004).

Hyperandrogenism

One of the symptoms of high androgens is hirsutism, as hair growth exceeds the normal limit on the face, chin, upper lip, abdomen, chest, legs, and lower back, and the appearance of acne (Ehraman, 2005). (Gallwey-Ferriman system) It is a system that describes the extent of hirsutism in a woman's body and depends on the presence of hair in 11 areas (Azziz et al ., 2008). Studies have shown that the cause of hirsutism is the increase in the level of androgens in the blood, especially the testicular lipid hormone in the blood, which is caused by an increase in the 5-α reductase enzyme (Greespan & Gardner, 2004).

As PCOS sufferers enter menopause, it has been found, their ovaries' activity decreases, and thus a decrease in the manufacture and secretion of female hormones from the ovary, but this will not reduce the condition of hirsutism, as well as increase baldness with age. Hair loss will appear, especially in the front of the head (El - Mazny et al., 2010), Acne is one of the most troublesome skin care problems and is a chronic inflammatory disease of the sebaceous capillaries (Dekkers et al ., 2006). It is also considered one of the hormonal disorders caused by androgens because women with PCOS suffer from a female hormonal imbalance that causes excessive male hormones, and patients have the highest percentage of Acne prevalence (Balen, 2007).

Excess androgens and their relationship to elevated non-alcoholic liver fat

An higher incidence of NAFLD in PCOS women may be caused by raised androgen levels, according to prior study (Kumarendran et al .,2018; Wu et al ., 2018) .Researchers found that testosterone levels were considerably higher in women with PCOS and NAFLD compared to people with PCOS alone (P .01) in a prospective study of Asian Indian women with PCOS. They concluded that hyperandrogenism is a distinct predictive factor for NAFLD. (Varma et al ., 2019). It is worth emphasizing that the researchers used serum testosterone levels as an androgen marker in this study. Because free testosterone or the free androgen index (FAI) assess bioavailable androgens more accurately, the link between androgens and NAFLD may be less if either is evaluated insteadreater FAI values were shown to be substantially (P =.002) linked with raise incidence of NAFLD when indices of free androgens were explicitly assessed in a research by (Vassilatou et al ., 2010), This illustrates how hyperandrogenism may directly contribute to the development of NAFLD and mimics the findings of the previous study.

According to a Chinese study, the incidence of NAFLD rise along with the FAI of Chinese women with PCOS (Cai et al ., 2017). Another study found a similar pattern: the highest quartile of FAI levels had the highest risk of liver damage, and liver damage was not just connected with rise androgen levels in PCOS women (Chen et al ., 2010). Thus, there is not only a definite link between hyperandrogenism and the risk of hepatocyte damage, but the risk appears to grow as androgen levels rise. An subsequent study discovered links between heightened FAI and NAFLD, eventually finding that women with hyperandrogenism have a distinct phenotype with a clearly rise risk of developing fatty liver disease. (Jones et al ., 2012). A study by (Falzarano et al., 2022) demonstrated that PCOS-related elevated androgen levels, insulin resistance, NAFLD is more common in women, It implies that these variables harm the liver more than fat does.

Infertility

When a man or woman is unable to conceive despite engaging in regular unprotected sexual activity for a period of 12 months or longer, they are said to be infertile.. (WHO, 2021). The ability of a man, woman, or spouse to engage in procreation (Akalewold et al., 2022). Infertility has psychological and social consequences such as stress, depression, and anxiety, and these factors have an impact on reproduction, and polycystic ovaries are a common cause of anovulation and infertility (Gurnee et al., 2009).Aging has a significant impact on fertility and fertility events (Tietz, 2006), as estrogen and progestogens (estrogens and progestins) and increased production of male hormones androgens cause hirsutism and acne (Bahri Khomami et al., 2019; Zehravi et al ., 2022).

Conclusion

According to research, PCOS has a substantial influence on women's reproductive and overall health, as this syndrome has a complex interweaving between genetic factors and hormones secreted by glands, the disruption of which leads to a defect or disruption of the function of organs. As women age, chronic diseases increase. Also, attention to accurate and early diagnosis of the syndrome works to speed up finding therapeutic solutions and reduce the damage of this syndrome.

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