



Reproductive Dysfunction in Women with PCOS: A Review Article

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Received: 26 January 2023

Accepted: 9 April 2023

Published: 20 April 2024

doi.org/10.30526/37.2.3246

Abstract

Polycystic ovary syndrome (PCOS) is a significant cause of infertility due to ovulation dysfunction in women of childbearing age. Although the pathogenesis of PCOS is still not clear, many studies have shown that many factors within the ovary promote infection. With this syndrome, the disruption of the natural monthly ovulation process causes an imbalance in the body's hormones, and the high level of insulin in the body and the blood sugar imbalance leads to the occurrence of hyperandrogenism, which is the main factor for the occurrence of pathogens, in addition to genetic factors, if any. This study aims to identify this disease and its most important causes, symptoms, and modern treatments to prevent and get rid of it. Polycystic ovarian syndrome is diagnosed based on the presence of anovulation associated with biochemical or clinical hyperandrogenism, and the new diagnostic criteria at the Rotterdam Conference 2003 are the basis for the diagnosis now. Obesity, infertility, irregular menstruation, recurrent miscarriage, and hirsutism are essential factors that must be treated to have a healthy pregnancy.

Keywords: Polycystic ovary syndrome, obesity, infertility, insulin resistant, metabolic disturbance.

1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common hormonal and genetic disorders in women; it was first described by Stein and Leventhal in 1935, and the incidence of the syndrome is estimated at 15–20% of women in the world of reproductive age, (15–20%) of women in the world of reproductive age (12–45) years. It is the leading cause of infertility, whether it is primary or secondary in women. About 26% of women with cysts are within primary infertility, 14% of them are within secondary infertility, 30% include a regular menstrual cycle, 50% suffer from infrequent menstruation, and 20% suffer from amenorrhea [1].



Polycystic ovary syndrome is a heterogeneous clinical condition in affected women. PCOS occurs in the vast majority of societies, and environmental, and genetic factors play a significant role in causing the disease. However, the primary cause of its incidence remains uncertain and imprecise. There are many clinical and chemo-biological features of the syndrome, including increased levels of hyperandrogenism, such as an increase in testosterone hormone than the standard limit, which causes infertility in most cases, hirsutism, and insulin resistance (IR) is also [2].

Insulin excess is one of the major metabolic disorders associated with women with the syndrome, as about 70% of women develop IR that develops into type 2 diabetes mellitus (T2DM). Heredity plays a significant role in causing the syndrome; a woman in her family has one or more people infected with the disease PCOS, such as a mother or a sister, who have a higher risk of developing PCOS than others [3].

2. The ovary

The reproductive system of the human being contains two important reproductive glands, the right, and left ovaries, which have two main functions: the production of eggs or zygotes and the production of ovarian hormones, which include estrogen, progesterone, and the relaxing hormone, as illustrated in **Figure 1**. The ovary is oval and consists of a shell, the Cortex Medulla; the cortex of the ovary contains ovarian follicles and the corpora lutea [4].

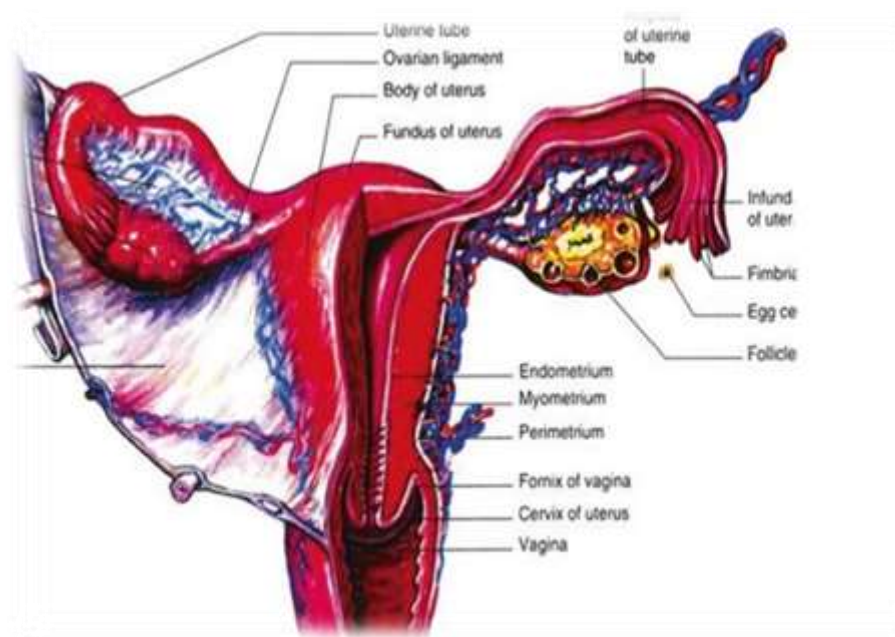


Figure 1. Front view of the female reproductive system [5].

This cortex is covered with a superficial epithelium. The tunic albuginea is a thick layer of connective tissue located directly under the surface epithelium; the tunica albuginea ruptures when the follicles and corpora lutea grow [6]. The medulla of the ovary is formed from the inner region, which contains a large number of blood vessels, nerves, and lymphatic vessels and consists of connective tissue and smooth muscles; the ovarian follicles are responsible for the formation of eggs and the secretion of estrogen, while the zero bodies secrete the progesterone hormone. The interstitial tissues found in the ovaries are responsible for the secretion of the relaxing hormone, quantities of luteinizing hormone, progesterone, and a small amount of androgens [7].

2.1 Types of follicles in the ovary of an adult female

The follicles in the ovary of an adult female consist of the precursor of the ovum Oogonium surrounded by a layer of ribbed epithelial cells representing granulosa cells, and the primordial follicles are covered by the basement membrane and located in the outer part of the ovarian cortex. Each ovary contains large numbers of primary follicles. These are the follicles that leave the resting stage as primary follicles to grow and develop as their cells undergo mitosis, thus increasing the number of their epithelial layers to become two or more layers of granular cells [8]. These follicles are also called vesicular follicles and consist of antral follicles and antrum, in which the zona transparent layer and the theca layer are distinguished. At this stage of follicle development, the ovary performs two essential actions: the formation of eggs and the secretion of hormones formed by the cells of the theca layer (estrogens and androgens). At the same time, the granulocytes are progesterin [9].

3. Polycystic ovary syndrome

Polycystic ovary syndrome is a complex, genetically heterogeneous disorder characterized by hyperandrogenism, the absence or absence of menstruation, hirsutism, and facial acne [10]. The face results in the most common cases of infertility among women of average reproductive age, as it is one of the most common hormonal diseases in various countries. Stein and Leventhal first described it in 1935. The incidence of the syndrome is estimated at (15-20%) of women in the world of childbearing age (12-45) years. It is the leading cause of infertility, whether primary or secondary, in women. About 26% of women with cysts are among those with primary infertility, 14% are among those with secondary infertility, 30% have a regular menstrual cycle, 50% suffer from a scarcity of menstruation, and 20% suffer from menopause [11]. The PCOS is a clinically heterogeneous condition in affected women, as the syndrome occurs in most societies, and environmental and genetic factors have a significant impact on causing the disease. Still, the leading cause of its occurrence is not known accurately or for sure. The syndrome has many clinical and biochemical features, including increased levels of androgenic hormones, such as an increase in testosterone levels above the standard limit, which causes infertility. In most cases, anovulation and hirsutism also cause IR. The rise in insulin is one of the significant metabolic functional disorders associated with women with the syndrome, as about 70% of them are exposed to IR that develops into T2DM [12]. Pathogenesis of POCS is illustrated in **Figure 2**.

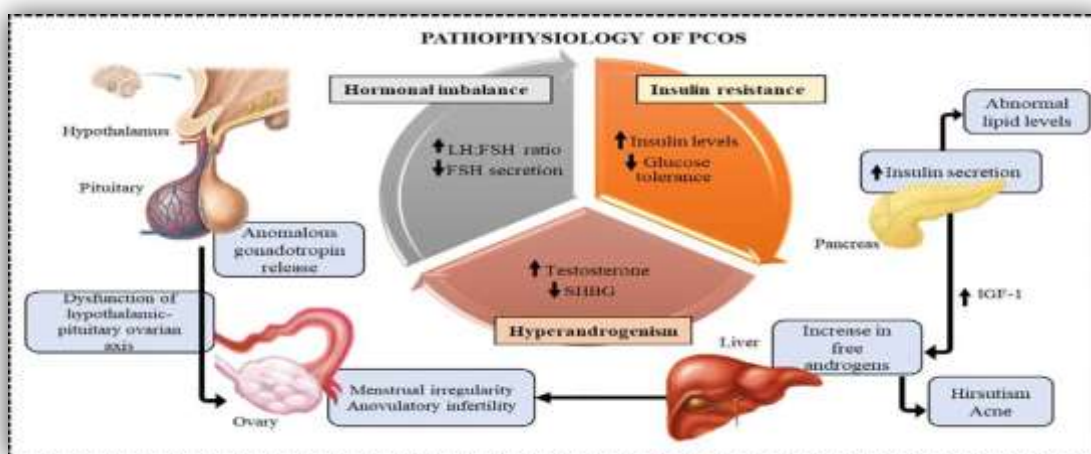


Figure 2. Pathogenesis of POCS [13].

3.1 Symptoms of polycystic ovary syndrome

3.1.1 Ovarian sacs

During the ultrasound examination of the ovaries of women with PCOS, a large number of sacs containing immature oocytes ranging in size (2-9) mm appear, as in each menstrual cycle, a sac grows to form a mature egg ranging in size (22-18) mm, but what happens is that a large number of cysts grow at one time, and then all of them stop unfolding in the middle of the road; therefore, none of these oocytes reaches the appropriate size and does not ovulate. An ultrasound scan shows an increase in the size of the ovary, and the cysts appear as pearl necklace beads, as shown in **Figure 3** [14]. When ovulation does not occur for some reason, the granulosa region of the ovary that surrounds the ovarian follicle self-destructs, leading to programmed cell death, known as apoptosis, which leads to the fragmentation of the follicle into pieces and its disappearance [15].

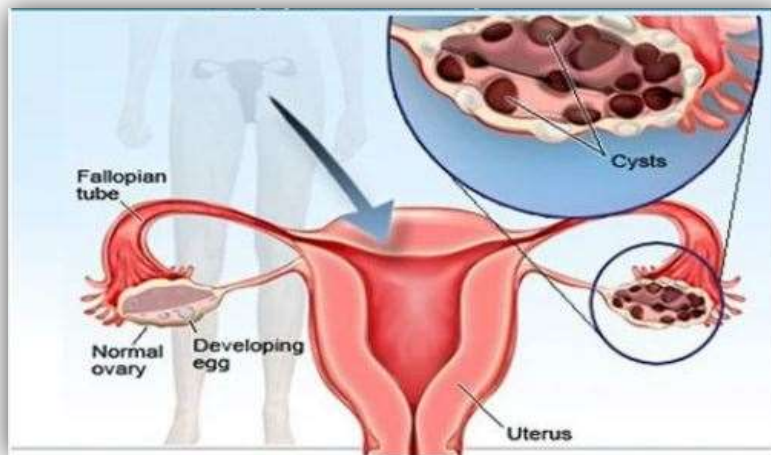


Figure 3. Ovarian cysts [16].

However, theca cell does not die and is preserved due to the high content of insulin, which prevents the follicle from disintegrating, which leads to the formation of an ovarian cyst. Theca cells produce the hormone androstenedione, and after a short period, the granulosa cells convert it to estrogen, while theca cells convert it to the testicular lipid hormone [17].

3.1.2 Infertility

Scientific infertility is defined as the failure to conceive after a full year of regular sexual intercourse and without the use of contraceptives or that pregnancy recurs in a woman. Still, it does not continue and does not include infertility resulting from surgery (such as removal of the ovaries) or the use of some medical treatments that have side effects on reproductive health, such as the use of chemotherapy and radiotherapy. The couple is not considered fertile unless the woman bears a whole child and is born alive, and the child produced is in good health [18].

The hormones of the hypothalamus, pituitary, and ovaries regulate the body's reproductive and physiological functions by stimulating some hormones and inhibiting others through the feedback mechanism. An imbalance in this hormonal balance leads to PCOS, which affects women, especially those of reproductive age [19].

3.1.3 Metabolic disturbances in women with polycystic ovary syndrome

Women with PCOS often have metabolic disturbances, such as decreased insulin secretion or decreased action. Insulin resistance with compensatory hyperinsulinemia is the main feature of PCOS and metabolic syndrome (MetS) [20].

Women with PCOS are usually at risk of developing T2DM; hyperandrogenism can be considered a pathogenic component of female MetS; and women with PCOS have an increased prevalence of multiple risk factors that increase the risk of cardiovascular diseases (CVD), such as high blood pressure (BP), obesity, T2DM, and dyslipidemia [21].

3.1.4 Insulin resistance

Normal glucose homeostasis is defined as a delicate balance between the effect of insulin in target tissues and insulin secretion by pancreatic β -cells. Skeletal muscle, liver, and adipose tissue are usually exposed to insulin. The development of insulin in skeletal muscle is estimated at 85% of the total amount of insulin. This is proportional to the amount of glucose taken, and the skeletal muscle is the critical target for glucose homeostasis. The adipose tissue is central to determining insulin sensitivity for the whole body [22].

The incidence of PCOS in women in the case of IR is above 70%; IR can be defined as a weak biological response to insulin with a state of compensatory hyperinsulinism, which makes patients vulnerable to poor glucose tolerance and T2DM. Studies have shown that 30%–40% of women with PCOS have poor glucose tolerance, and 10% develop T2DM at the age of 40—defects in insulin secretion and reduced hepatic insulin clearance in the blood attributed to this condition. Insulin resistance is the key to many pathophysiological features of PCOS, causing many disorders in the reproductive and metabolic processes. Insulin stimulates androgen production in the ovaries and decreases hepatic (SHBG) formation by increasing free, total, and heterogeneous androgens [23].

3.1.5 Obesity

Women with PCOS are more likely to develop obesity than other women worldwide. The prevalence of overweight and obesity in women with PCOS varies between countries and ethnic groups, ranging between (60-80%) of obese women with PCOS showing lower levels of SHBG and higher levels of free androgen compared with their counterparts of average weight. It was found that the distribution of body fat affects the concentration of (SHBG) and androgens, and obesity negatively affects reproductive function in a significant way, independent of women with PCOS [24]. Obese women with PCOS have more difficulty conceiving and are less responsive to ovulation-inducing drugs. Obesity and adipose tissue-related factors can be critical in inducing and perpetuating PCOS [25].

Obesity is usually associated with IR, and body fat distribution is a qualitative indicator of metabolic irregularities. Among the metabolic imbalances related to IR are high plasma glucose, problems regulating fats, high triglycerides, and increased low-density lipoprotein decreased high-density lipoprotein, as well as high BP and the effect on the state of pre-coagulation prothrombic and obesity. These problems and imbalances in metabolism stimulate the occurrence of T2DM, atherosclerosis, and heart disease [26, 27]. **Figure 4** shows a summary of mechanisms linking obesity with PCOS.

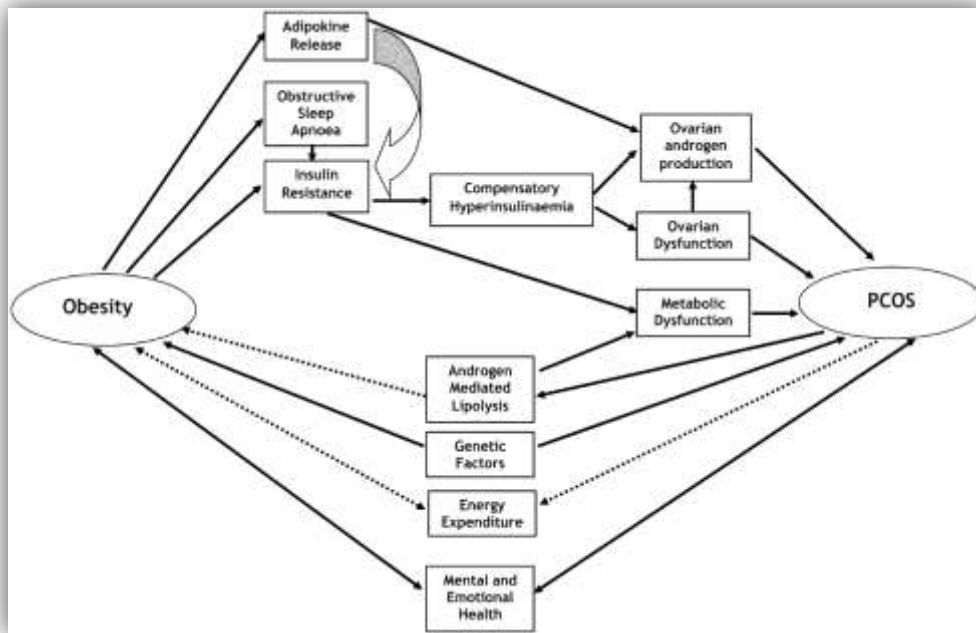


Figure 4. Summary of mechanisms linking obesity with PCOS [28].

4. Treatment of polycystic ovary syndrome

Fertility drugs have been widely used since the beginning of the 1960s, the most important of which is metformin; this medication is safe, effective, and has benefits and a unique treatment available [29]. In others, metformin stimulates the processes of ovulation and egg formation, as studies have shown its effectiveness through a decrease in glucose formation in the liver with a reduction in the rate of carbohydrate absorption in the intestine, as it reduces the level of glucose in the blood by increasing insulin sensitivity without increasing the concentration of insulin [30]. It also improves the menstrual cycle and its regularity in many women with PCOS syndrome, as well as reducing the miscarriage rate for women with PCOS, which is an ideal treatment for women who want to become pregnant and give birth, and when combined with exercise and a healthy diet in about six months [31, 32].

5. Conclusion

Obesity, infertility, irregular menstruation, frequent miscarriages, and hirsutism are essential indicators of PCOS. Family history plays a vital role in developing the syndrome. Early diagnosis of the disease, adherence to diet and exercise, and adherence to the doctor's recommendations are crucial in preventing complications associated with PCOS.

Acknowledgment

The authors thank the Department of Chemistry/ College of Education for Pure Science (Ibn Al-Haitham) at the University of Baghdad for review approval.

Conflict of Interest

There is no conflict of interests.

Funding

There is no financial support.

Ethical Clearance

This work has been approved by the Scientific Committee at the University of Baghdad/ College of Education for Pure Science (Ibn Al-Haitham).

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