Polycystic Ovarian Syndrome and Pregnancy Complications

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Abstract:
Polycystic Ovarian Syndrome is now a common endocrine disorder leading to reproductive disorder during reproductive age. The disorder not only effect women health but also affect their quality of life. Early diagnosis of the disorder is very important because this can remain unidentified for long period of time due to no specific diagnosis criteria. With increasing age, the evolves from reproductive disorder to metabolic disorder. The metabolic disorder may include hormonal imbalance and development of type 2 diabetes and cardiovascular diseases. The disorder is the major cause for anovulatory infertility. Environmental factors such as life style and diet and obesity also contribute to the disorder. Different women may show diverse symptoms and not all women suffering from PCOS have ovarian cyst. The disorder may also show psychological changes like anxiety, depression and obsessive compulsion disorder.

Keywords: *PCOS, reproductive disorder, endocrinology, hyperandrogenism, anovulatory infertility, hormonal imbalance, gestational diabetes mellitus, type 2 diabetes*

1. Introduction

Polycystic Ovarian Syndrome commonly known as PCOS is one of the major reproductive disorders occurring in females of reproductive age. It is a serious endocrine disorder which has no permanent cure but only can be limited and kept under control. According to the survey of about one in five women in India is affected by the disorder but is usually left unattended. The root cause for PCOS is imbalance of various hormones in body. Earlier PCOS was defined as symptoms complex due to anovulation. With time the symptoms and criteria foe diagnosis broadened. The disorder has no defined symptoms rather the symptoms vary with people making the diagnosis difficult. PCOS has reproductive, psychological and metabolic features.

Reproductive symptoms include irregular menstrual cycles, hirsutism, subfertility and pregnancy complications. The psychological features include anxiety depression low self esteem and obsessive compulsion disorder (OCD). With time the reproductive features lead to metabolic disorders such as insulin resistance causing high glucose level in body and leading to type 2 diabetes, dyslipidemia and cardiovascular risks. The psychological disorder is not specified symptoms but are also result of PCOS.

Early and timely diagnosis of the disorder and appropriate strategies to keep type 2 diabetes, hypertension also cardiovascular risk under control is of utmost importance. Healthy lifestyle better eating habits and regular checkup can help to keep PCOS under check. PCOS diagnosis is based on the Rotterdam consensus meeting in 2003 stating 2 features – 1) oligo-ovulation or anovulation accompanied by irregular menstrual cycles. 2) hyperandrogenism (signs including hirsutism).

2. Adolescence

As a result of ovulatory dysfunction, irregular periods are the key symptom of PCOS. A normal menstrual cycle varies from 21 to 45 days with average cycle of 28 days is very common in adolescent girls. Irregular cycles are common during pubertal transition. Hence it makes it difficult in adolescent

girls to differentiate between normal pubertal development and signs of PCOS. Half of the cycles range from 21 to 45 days during second year of menarche and almost majority of irregular cycles are anovulatory. It is said that with increasing year following menarche only few females experience cycle exceeding 45 days. The studies show that girls who are less than 2 years after menarche with features suggesting PCOS are on high risk of PCOS.

Ascertainment of hyperandrogenism can be difficult. Hyperandrogenism can be clinical causing acne and hirsutism or biochemical, which is high circulating androgen level. Not all cases of hirsutism are associated with high androgen level. Acne prone skin is very common in puberty, androgen level increase physiologically is characterized by acne in teenager. To calculate androgen level assess to biochemical hyperandrogenism can be used.

Polycystic Ovary Morphology (PCOM) is defined as >12follicles with the diameter o 2-9mm in ovary or ovary volume of >10 mL. As multicystic ovaries are common during puberty, PCOM is not used as a criteria for PCOS diagnosis. However, studies show that women with eumenorrheic women with PCOM have higher androgen level that normal eumenorrheic females, suggesting they might be at risk for anovulation later in life.

3. Hormonal imbalance and irregular ovulation

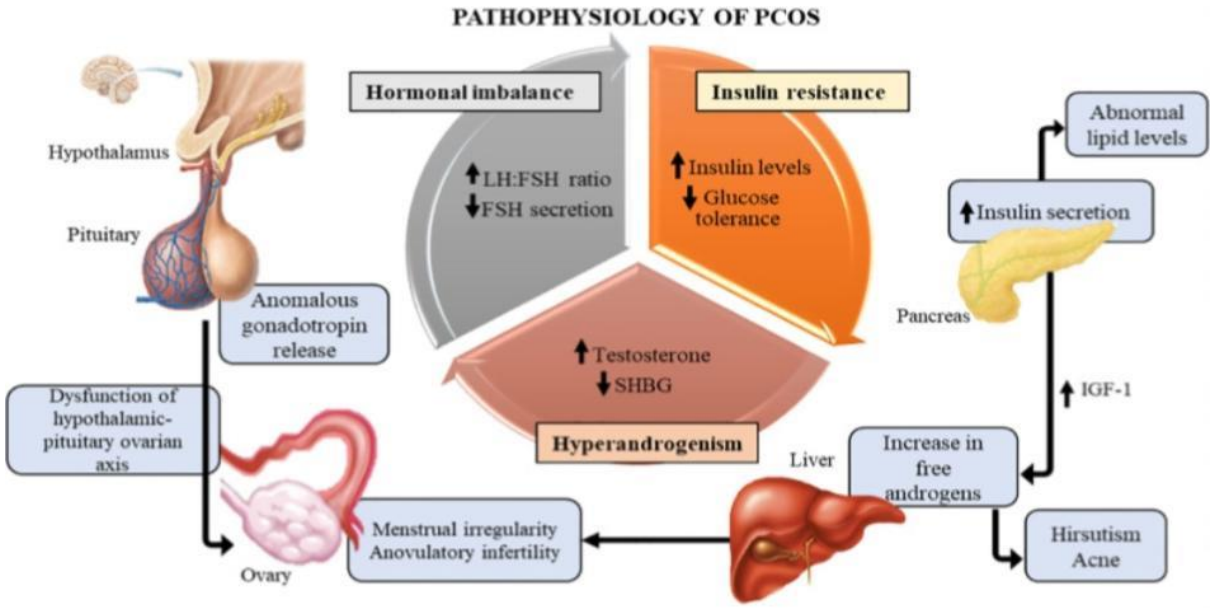
The pathophysiology of PCOS is not clear; however, disturbance in hypothalamic-pituitary-ovarian axis and abnormal steroidogenesis along with genetic and environmental factors act as main contributors to this disorder.

Hormones are chemical messenger that are released by endocrine glands for specific functions. Polycystic ovary is ovaries with multiple number of cysts. This is mainly due to hormonal imbalance. Human ovaries contain number of immature eggs stored in them which get matured when puberty hits and are released every month from alternate ovaries. Immature ovaries are stored in follicles. Pituitary gland i.e. master gland stimulate GnRH (Gonadotropin release hormone) to release hormones FSH (Follicle stimulating hormone) and LH (luteinizing hormones). These hormones through blood reach to ovaries and initiate egg release from follicles. This process is termed as ovulation. The GnRH pulse frequency regulate the level of LH And FSH. Both the hormones are released in equal amount. Luteinizing hormone acts primarily on the ovarian theca cells carrying LH receptors and induces the production of androgens. Concomitantly, FSH acts on the ovarian granulosa cells and converts the androgens formed in theca cells into estrogens, principally estradiol, which is responsible for the development of follicles.

Progesterone is female hormone released in ovaries by corpus luteum. Progesterone has negative (-)ve feedback effect on GnRH. When ovulation fails to occur no Progesterone is released which stimulate GnRH negatively and an abnormal condition is developed where the LH and FSH levels are disturbed. GnRH starts to produce more amount of LH and less amount of FSH. As both these hormones help in ovulation of eggs, their disturbed levels lead to failure in follicle maturation to point of ovulation. Follicles that fail to ovulate form fluid filled **cysts. Cysts** in ovaries represent past failed ovulation events.

Increased LH reach the **thecal** cells of ovaries and tend to release high amount of male hormone-**androgen. Thecal cells** are endocrine cells associated with ovarian follicle that play an essential role in fertility by producing androgen required for ovarian estrogen biosynthesis. Androgens are a group of sex hormones. They help start puberty and play a role in reproductive health and body development. All genders make androgens, but males make more of them. Testosterone is the most common androgen. Females produce very little amount of androgen but its amount increases and leads to issues like **hirsutism, acne, menstrual irregularities and also infertility** (no ovulation). This increased amount of androgen is termed as **hyperandrogenism.**

Insulin hormone released by pancreas also leads to **steroidogenesis in thecal cells** which also leads to increase in androgen levels. Androgen also has (-)ve feedback on hypothalamus which increases hormonal imbalance and complications in ovulation. Androgen causes decrease in **insulin sensitivity** and hence more insulin is released. This is called **insulin resistance.** This leads the person more susceptible to Type2 diabetes mellitus. Insulin resistance leads to more insulin release and thecal cells are forced to release more androgen. This whole process is a cycle.



Source- www.sciencedirect.com

4. Endocrine Factors

Folliculogenesis is basically development of female germ cell into fertilizable egg within the somatic cells of the ovary. Arrest of follicle growth is a result of various extra- and intra- ovarian factors. Disturbance in the factors alter the follicle development, formation of oocyte and leading to infertility.

5. Extraovarian Factors-

Extraovarian factors include disturbed level of endocrine hormone leading to follicular arrest. Factors such as high androgen level, FSH deficit, hyperinsulinemia and insulin resistance. FSH role is recruit ovarian follicles and stimulate their growth and LH in females triggers release of eggs from ovary. In normal females FSH levels are high and LH levels are low. In PCOS females due to endocrine disturbance the FSH level is low and high LH level is noticed. In normal cycle only the dominant follicle responds to LH when follicle size increases to 10mm in diameter whereas in PCOS females' small follicles react to LH. LH in these women promote early luteinizing of granulosa cells and lead to early arrest of antral follicles.

6. Intraovarian Factors

Folliculogenesis and oogenesis also depend upon intraovarian factors such as follicular fluid factors FFFs. Some intraovarian factors are

7. Epidermal Growth Factors (EGF)

In human ovary, EGF is present in follicular fluid FF, where it regulates follicle development and oocyte maturation. In OCOS females EGF level in FF is higher than the normal women. High EGF may inhibit oestrogen synthesis leading to arrest of follicle growth.

8. Neurotrophin Growth Factor (NGF)

NGF plays a fundamental role in folliculogenesis and oocyte maturation. It promotes nuclear and cytoplasmic maturation of oocyte, and processes development of good quality oocyte and embryos. In PCOS females' high level of NGF is noted.

9. Inhibin

Inhibin and activin are polypeptides found in follicular fluid of ovary. Inhibin tends to inhibit FSH secreation, which is important for growth of eggs and it stimulates egg production. In PCOS females elevated level of inhibin is recorded. Inhibin shows negative feedback on FSH secretions.

10. Anovulatory cycles

the typical indication of PCOS is anovulatory cycles. Anovulatory cycles may either be oligoamenorrhea – menstrual cycles of more than 35 days or secondary amenorrhea – absence of cycles for as long as three months and more. Polymenorrhea condition may also develop, frequent cycles with an interval of less than 24 days. Menstrual irregularities often begin after menarche and decrease when approaching menopause. This correlated to a decline in androgen levels with advancing age in women with PCOS. 95% of adult women with PCOS have amenorrhea.

11. Ultrasonographic features

Ultrasonographic evidence of polycystic ovaries is one of the major criteria of the Rotterdam guidelines 2003. The diagnosis criterion include presence of 12 or more follicles of diameter 2-9mm or ovarian volume of more than 10 ml. about more than 80%of women with PCOS show polycystic ovaries and morphological changes in ovary. Normal females may also show symptoms of polycystic ovary. The cause of polycystic ovaries may be also due to hyperprolactimenia and hypothalamic amenorrhea.

12. Fertility and Pregnancy Complications

PCOS is the main cause of subfertility in 70% of females. Several meta-analysis report pregnancy and delivery complications in women with PCOS. it includes increased risk of Gestational Diabetes Mellitus (GDM), gestational hypertension pre-eclampsia (PE) and cesatrean section most common in women with PCOS. these problems expose women to higher risk of premature delivery also. Studies also report the babies from women diagnosed with PCOS are 4 times more often small for gestational age.

PCOS diagonised females have 30 – 50% chances of miscarriage, which is higher than in normal females.

13. Conclusion

PCOS is a complex disorder which involves endocrine, environmental genetic and behavioral aspects interlinked and posing a serious disorder in reproductive females. The disorder shows varied symptoms in different females hence diagnosis is difficult. PCOS can cause serious health issues and is a serious cause of infertility in females. It affects the quality of life in females and increases the risk of miscarriage in pregnant females. Timely and early diagnosis is very important for treatment.

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