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Relation between Obesity and PCOS (Polycystic Ovarian Syndrome) in Today's Life

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ABSTRACT

Both obesity and polycystic ovary syndrome (PCOS) are the raising epidemics in the world today. Polycystic ovarian syndrome (PCOS) is one of the most leading causes of female infertility, affecting 5-10% of women of reproductive age. The syndrome is characterized by anovulation, hyperandrogenism and polycystic ovaries. Obesity (defined as a BMI ≥ 30 kg/m²) occurs in approximately 30% to 60% of women with PCOS. Central or abdominal obesity is a typical pattern. Central obesity is a risk factor for development of diabetes, heart disease and when present in a woman with PCOS worsens the clinical features of the syndrome. Obesity may play a pathogenic role in the development of the syndrome in susceptible individuals. Therefore lifestyle modifications with appropriate diet and exercise is a corner stone of therapy for many women with PCOS.

INTRODUCTION

Obesity may be defined as abnormal growth of adipose tissue or fat cells that is enlargement of fat cell size (Hypertrophic obesity) or increase in fat cell number (Hyperplastic obesity) ⁽¹⁻⁵⁾. Obesity is a multisystem disorder which involves respiratory system, cardiovascular system etc., (Figure 1).



Figure 1: Obesity

Obesity is a key risk factor of other diseases like pcos (Polycystic ovarian syndrome) and diabetes mellitus. Obesity is difficult to treat. People with obesity when they lose weight they have a chance to gain weight within five years. Stress is an important factor that triggers obesity (5-10). Stress is produced factors that impose excessive demands on the body altering homeostasis. It can affect one's physical, as well as psychological health problems resulting in depression, sleeplessness, insomnia and changes in eating patterns that promote increasingly abnormal health states (10-15).

There are 2 types of obesity. They are:

Android obesity (or) Central Obesity (Apple shape)

Android obesity is a type of obesity in which the fat is stored in the abdominal region (15-20). It can be seen in areas like upper chest, shoulders, neck etc., It is seen most commonly in men (21-30) (Figure 2).

Gynoid Obesity (Pear shape)

Gynoid obesity is characterized by presence of fat at hip, thigh and Buttocks region. It is seen most commonly in women.

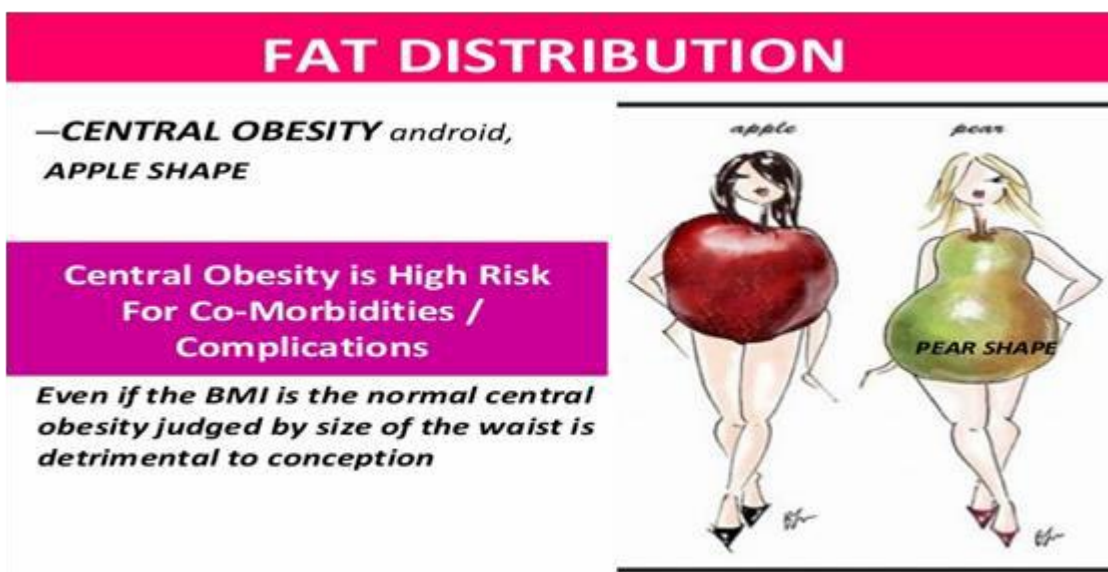


Figure 2: Central Obesity

If a person's bodyweight is 20% higher than the normal, that condition is to be obese (31-40). When the Body Mass Index (BMI) ranges from 25 to 29.9 it says that the person is overweight (Table 1). If BMI is 30 or more then it is said to be obese (41-50).

$$\text{BMI} = \text{Weight (kg)} / \text{Height (m}^2\text{)}(1)$$

BMI	BMI Categories
Below 18.5	Underweight
18.5 to 24.9	Normal
25.0 to 29.9	Overweight
30.0 and above	Obese

Table 1: Body Mass Index

Why Do People Become Obese?

People can become obese for many reasons. The most common ones are:

- Consuming too many calories.
- Leading a sedentary lifestyle
- Alteration in sleeping patterns
- Endocrine disruptors, such as some foods that interfere with lipid metabolism
- Medications that make patients put on weight
- Diseases such as hypothyroidism, PCOS (polycystic ovarian syndrome), insulin resistance and Cushing's syndrome.
- Psychological symptoms such as stress, anger, boredom etc

Being Obese Can

- Increase blood cholesterol and triglyceride levels.
- Decrease "good" HDL cholesterol.
- Raise blood pressure
- Depression
- Overweight girls may have irregular menstrual cycles and fertility problems in adulthood.
- Lead to diabetes

When Your Weight is in a Healthy Range?

- When your body more efficiently circulates blood.
- When your fluid levels are more easily managed.
- When your body prevents the development of diabetes, heart disease, certain cancers and sleep apnea.

Polycystic Ovarian Syndrome (PCOS)

Polycystic ovarian syndrome (PCOS) is a syndrome characterised by oligomenorrhoea^(51,52), anovulation, infertility, hirsutism, and obesity in young women having bilaterally enlarged and cystic ovaries. In PCOS there is a presence of large cysts in the ovaries, Hence it is named as polycystic ovaries⁽⁵³⁻⁶⁰⁾.

In 1935, Stein and Leventhal reported the classic symptomatology in a group of women who had amenorrhoea, infertility⁽⁶¹⁻⁷⁰⁾, hirsutism, and enlarged polycystic ovaries. It affects the women aged 20-44 years.

Aetiology

- The principal biochemical abnormalities in most patients are excessive production of androgens, and low levels of pituitary follicle stimulating hormone (FSH). These abnormalities will lead to ovarian dysfunction.
- Mainly pcos is caused by unbalanced release of FSH and LH by the pituitary.
- Hereditary basis for the syndrome has been suggested in some cases.
- Menstrual irregularities are observed in women with PCOS.
- Obese people are more likely to have menstrual irregularity and an ovulatory infertility than normal weight women ⁽⁷¹⁻⁸⁰⁾.
- In reproductive age women, the relative risk of ovulatory infertility increases at a BMI of 24 kg/m² and continues to rise with increasing BMI. Weight reduction can restore regular menstrual cycle in the women.
- In PCOS bioavailable androgen levels are increased. The abnormality is further worsened by obesity, especially central obesity, finally sex hormones ⁽⁸¹⁻⁸⁶⁾ binding globulins levels are reduced in this state due to hyperinsulinemia.
- In women with PCOS, multiple small follicles accumulate in the ovary, hence the term polycystic ovaries.

Pathophysiology

The pathophysiology of PCOS is complex. The primary defect in PCOS is unknown, but at least three potential mechanisms acting alone or synergistically, appear to create the characteristic clinical presentation. These mechanisms include:

Gonadotropin Secretion

In PCOS, there is an increased frequency of GnRH stimulation, leading to an increase in LH pulse frequency and amplitude, while FSH secretion remains normal. the development of dominant follicle does not occur because LH secretion occur to early in menstrual cycle. Therefore, a woman is left with several immature follicles and usually will not ovulate. Increased LH stimulation also leads to increased steroidogenesis in the ovary, leading to excess androgen production.

Excess Androgen Production

Androgen production occurs in the theca cell of the ovary to facilitate follicular growth and estradiol synthesis in the granulosa cell. In women with PCOS, hyper secretion of LH and insulin increase the production of androgens, causing abnormal sex steroid synthesis, hyperandrogenism, hyperandrogenemia ⁽⁸⁷⁻⁹⁰⁾.

Theca cells in women with PCOS are more efficient at the conversion to testosterone than normal theca cells. When hyperandrogenism or hyper insulinemic states exist , androgen production is further enhanced.

Insulin

Women with PCOS generally exhibit an increased risk of insulin resistance with compensatory hyperinsulinemia. Insulin resistance is associated with reproductive and metabolic abnormalities in women with PCOS and can occur in both obese and non obese women. This occurs mainly due to defects in insulin- receptor signalling which leads to insulin resistance ⁽⁹¹⁻⁹⁵⁾.

Insulin has both direct and indirect roles in PCOS. In the ovary, insulin acts alone or synergistically with LH to increase androgen production in theca cells.

Clinical Features

Signs and symptoms of PCOS usually begin at the time of puberty, although some women do not develop symptoms until late adolescence because of hormonal changes.

Common clinical signs of pcos include :

- Thick pigmented body hair in a male pattern distribution and commonly found on the upper lip, lower abdomen, and around the nipples.
- Hirsutism
- Acne
- Alopecia
- Menstrual irregularity
- Weight gain and obesity
- Insulin abnormalities like insulin resistance and hyperinsulinemia
- Infertility
- Sleep apnea
- Heart diseases
- Hirsutism is the most common of these features occurs in 60% to 75% of a women with PCOS.

Diagnostic Criteria

There is no single test for diagnosing polycystic ovary syndrome (PCOS). You may be diagnosed with PCOS based upon your symptoms, blood tests, and a physical examination

Major diagnostic criteria for PCOS have been proposed by different organizations. The diagnostic criteria include:

- Hyperandrogenism (clinical signs) or hyperandrogenemia (biochemical signs)
- Oligo-ovulation (irregular ovulation)
- Other disorders like thyroid abnormalities, hyperprolactinemia etc.
- Polycystic ovaries on pelvic ultrasound

If PCOS is confirmed, blood glucose and cholesterol testing are usually performed. In women with moderate to severe hirsutism (excess hair growth), blood tests for testosterone and dehydroepiandrosterone sulfate (DHEA-S) may be recommended.

All women who are diagnosed with PCOS should be monitored by a healthcare provider from time to time.

TREATMENT

Non Pharmacological Treatment

- Weight reduction
 - Decreasing body weight 5-10% significantly reduces hyperandrogenism, insulin resistance and anovulation
 - Incidence of eating disorders higher in PCOS
- Psychotherapy
- Hair removal

- Shaving
- Chemical bleaching and waxing
- Laser removal
 - Diet composition
 - Exercise

Pharmacological Treatment

Combined oral contraceptives

Estrogen-progestin combination therapy with a combined oral contraceptives is the treatment of choice for women seeking regularity in menstrual cycles and relief from hyper androgenic symptoms. The estrogen component suppresses LH, resulting in a reduction of androgen production, and increase hepatic production of SHBG (sex hormone binding globulin), thereby reducing free testosterone ⁽⁹⁶⁻¹⁰⁰⁾.

Caution should be used in those who have insulin resistance, a high propensity to develop type-II diabetes, or abnormal lipid profiles.

General side effects of combined oral contraceptives include breast tenderness, breakthrough bleeding, mood swings, libido changes.

AGENTS FOR OVULATION INDUCTION

Clomiphene Citrate

Clomiphene citrate induces ovulation via an antiestrogenic effect on the hypothalamus. GnRH secretion is increased, which increases LH and FSH production.

The increase in FSH concentrations causes appropriate follicle development and estrogen secretion, which produces positive feedback on the hypothalamic-pituitary system to create a LH surge for ovulation^[6]. The combination of Clomiphene citrate plus metformin initially produced higher ovulation rates than either agent alone. Long term cyclic therapy beyond a total of six cycles may lead to potential ovarian cancer. General side effects include vasomotor symptoms, gastrointestinal problems ⁽¹⁰¹⁻¹⁰³⁾.

INSULIN SENSITIZERS

A reduction in insulin levels by using insulin sensitizers can ameliorate the sequelae of hyperinsulinemia and hyperandrogenemia.

Metformin

Metformin was statistically significantly better in women with PCOS for ovulation induction when compared to rosiglitazone.

Metformin acts by inhibiting hepatic glucose output, providing lower insulin concentrations and reduces androgen production in the ovary. It also appears to influence ovarian steroidogenesis.

General side effects of metformin include gastrointestinal problems, diarrhoea, abdominal pain.

Thiazolidinediones

These agents improve insulin action in the liver, skeletal muscle and adipose tissue. They also directly affect ovarian steroid synthesis.

General side effects of thiazolidinediones include edema, head ache, fatigue, weight gain.

AGENTS FOR HIRSUTISM

Spironolactone

It acts by competitively inhibiting dihydrotestosterone from interacting with its androgen receptors. This causes decrease in activity of ovarian produced testosterone. It reduces hair growth by 40-80%.

General side effects of spironolactone include polymenorrhoea (if administered as monotherapy), head ache, fatigue, hyperkalemia.

Finasteride

It is a type II 5 α -reductase inhibitor which decreases the conversion of testosterone to dihydrotestosterone. It provides an approximate 30% reduction from baseline for hirsutism. Compared to spironolactone it has less effectiveness in women with hirsutism.

CONCLUSION

Weight gain is an important contributor (both genetic and environmental) in women with polycystic ovarian syndrome. Obesity in women does not always results in the development of PCOS. So it is incorrect to state that obesity causes pcos. Obese women with PCOS experience greater menstrual irregularity when compared to non-obese patients. Therefore exercise and diet modifications are the front line therapy for the management of PCOS.

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