Effect of Polycystic ovary syndrome (PCOS) in Indian women of reproductive age -A review article

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Abstract

Introduction:-Polycystic ovary syndrome (PCOS) is a problem with hormones that affects women during their childbearing years (ages 18 to 44). Between 2.2 and 26.7 percent of women in this age group have PCOS, Many women have PCOS but don't aware of it. In one study, up to 70 percent of women with PCOS hadn't been diagnosed. PCOS affects a woman's ovaries, the reproductive organs that produce estrogen and progesterone — hormones that regulate the menstrual cycle. The ovaries also produce a small amount of male hormones called androgens.

Aim: - The aim of the present review is to provide a comprehensive view of the literature regarding the association of polycystic ovary syndrome (PCOS) in reproductive age group women 18-35 years.

Results:- In Correlation of polycystic ovary syndrome (PCOS) with Reproductive Health Problem, the various studies results show that ovarian radiologic evidence of PCOS in as many as 40% to 80% of recurrent pregnancy loss patients. Many women with PCOS have metabolic alterations in glycemic control characterized by insulin resistance. Patients with thyroid disease often have concomitant reproductive age abnormalities, including ovulatory dysfunction and lute phase defects. The metabolic demands of early pregnancy mandate an increases requirement for thyroid hormonals. It is therefore not surprising that hypothyroidism has been associated with isolated spontaneous pregnancy loss and recurrent pregnancy loss.

Conclusion: In reproductive age women with PCOS have reproductive health problems like menstrual irregularities, polycystic ovarian syndrome, miscarriages and infertility hormonal changes. Hence thyroid function test should be routinely recommended for all women in reproductive age as it helps in early detection of hypothyroidism that can be treated medically with hormones and is cost-effective. Unnecessary surgery can be avoided in menstrual irregularities like menorrhagia and complications of pregnancy can be prevented which will reduce burden on the health system and society

**Key Words: Polycystic ovary syndrome (PCOS), Women in India,**

Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder affecting 5–10 % of women of reproductive age. Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder, leading to several health complications, including menstrual dysfunction, infertility, hirsutism, acne, obesity, and metabolic syndrome. However, its pathophysiology remains largely unknown but many believe that PCOS appears to be familial, with its various aspects differentially inherited from one generation to the next. Although more than 100 candidate genes have been investigated, and the potential for gene discovery to improve diagnosis and treatment of PCOS is promising, there is much to be done before the current findings can be applied in clinical practice. The three major diagnostic criteria of PCOS widely followed are criteria raised by National Institutes of Health (NIH), 2003 Rotterdam Consensus raised by European Society of Human Reproduction and Embryology (ESHRE) and American Society for Reproductive Medicine (ASRM) and criteria raised by Androgen Excess Society (AES).The manifestations of PCOS are not confined to the gynecological sphere; women afflicted by this disease show an increased prevalence of several comorbidities, including obesity, dyslipidemia, hypertension, metabolic syndrome (MS), and type 2 diabetes mellitus (DM2) in comparison with women without PCOS. These features, along with other alterations such as endothelial dysfunction and a chronic low-grade inflammatory state, underlie the greater risk of developing cardiovascular disease and increased all-cause mortality observed in these subjects.
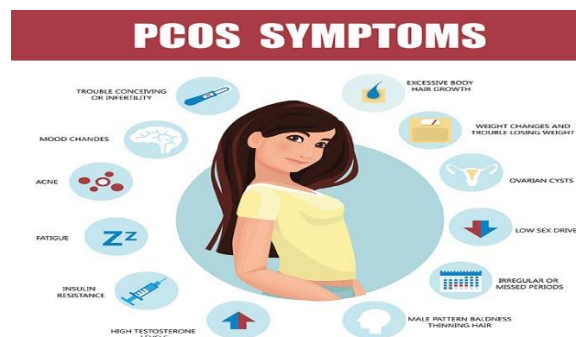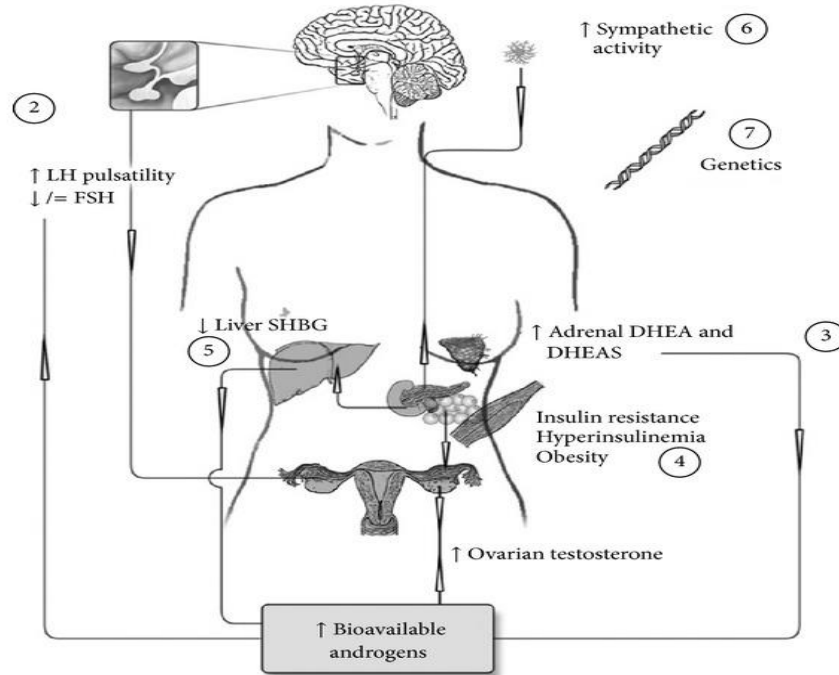
Common symptoms of PCOS include:

- Irregular periods or no periods at all.
- difficulty getting pregnant (because of irregular ovulation or failure to ovulate)
- Excessive hair growth (hirsutism) – usually on the face, chest, back or buttocks.
- Weight gain.
- Thinning hair and hair loss from the head.
- Oily skin or acne.
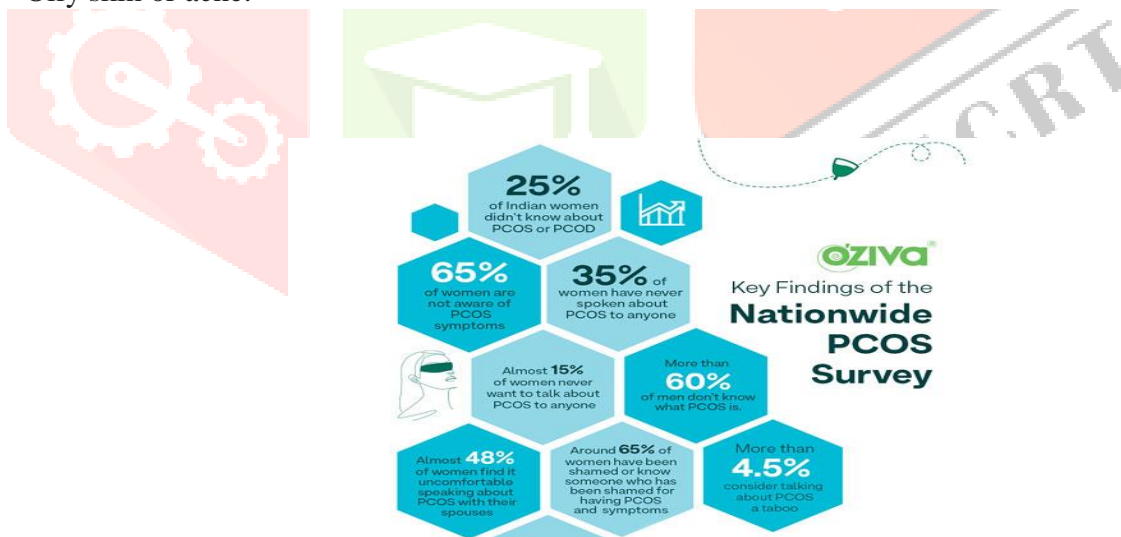
65 percent women in India unaware of PCOS symptoms; revels survey conduct by oziva

Ultrasound images: A polycystic ovary and a normal ovary

Polycystic ovary with many antral follicles

Normal ovary with a single mature follicle Yellow cursors are measuring the frolics

Review of literature

Cibula et al (2000) selected 28 women with PCOS from a large group who had undergone ovarian wedge resection between 1960 - 1981 (PCOS group - typical appearance of PCO on histology followed by a questionnaire study: menstrual history - oligomenorrhoea > 45 days or amenorrhoea; hirsutism - Ferriman and Gallwey score > 8; an ovulatory infertility; biochemical assay) and compared them to 752 control women selected by age (45 - 59 years) from a random female population sample. There was no difference in BMI, waist circumference, or W/H between the two groups. Both groups had comparable family histories with respect to type II diabetes, hypertension, coronary artery disease, and smoking habits. Overall the prevalence of type II diabetes was higher in women with PCOS and was four-fold higher in women with PCOS aged 45 to 54 years (p < 0.05).

Legro et al (1999) studied 254 women with PCOS (ages 14-44 years; unexplained hyper androgenic chronic anovulation with a history of irregular menses and elevated serum T levels) prospectively at two centers; one urban and ethnically diverse (n = 110), and one rural and ethnically homogenous (n = 144). The control group comprised 80 weight, ethnicity, and age-matched women from the same areas. The prevalence of glucose intolerance (31.1%) and type II diabetes (7.5%) was significantly higher in women 53 with PCOS. In non-obese PCOS women (BMI < 27 kg/m2) the prevalence of glucose intolerance and diabetes was 10.3% and 1.5% respectively. Variables that were most associated with post-challenge serum glucose levels were fasting serum glucose (p = 0.0001), PCOS status (p = 0.002), W/H (p = 0.001) and BMI (p = 0.021). The authors suggest that PCOS women are at increased risk of impaired glucose tolerance and type II diabetes at a young age, and that PCOS may be a more important risk factor than ethnicity or race for glucose intolerance in young women.

Ehrmann's (1999) study lacks follow-up of all women. At baseline nearly half (45%) of PCOS women had an abnormal glucose tolerance. Although one cannot determine causality, this suggests that the prevalence of abnormal glucose tolerance is high in PCOS women.

Richard S. Legro, William D. Schlaff, Michael P. Diamond, (2010) Objective: The aim was to compare assay results from a direct RIA with two LC/MS.**Design and Setting:** We conducted a blinded laboratory study including masked duplicate samples at three laboratories—two academic (University of Virginia, RIA; and Mayo Clinic, LC/MS) and one commercial (Quest, LC/MS).**Participants and Interventions:** Baseline testosterone levels from 596 women with PCOS who participated in a large, multicenter, randomized controlled infertility trial performed at academic health centers in the United States were run by varying assays, and results were compared.**Main Outcome Measure:** We measured assay precision and correlation and baseline Ferriman-Gallwey hirsutism scores.**Results:** Median testosterone levels were highest with RIA. The correlations between the blinded samples that were run in duplicate were comparable. The correlation coefficient (CC) between LC/MS at Quest and Mayo was 0.83 [95% confidence interval (CI), 0.80–0.85], between RIA and LC/MS at Mayo was 0.79 (95% CI, 0.76–0.82), and between RIA and LC/MS at Quest was 0.67 (95% CI, 0.63–0.72). Interassay variation was highest at the lower levels of total testosterone ($\leq$50 ng/dl). The CC for Quest LC/MS was significantly different from those derived from the other assays. We found similar correlations between total testosterone levels and hirsutism score with the RIA (CC = 0.24), LC/MS at Mayo (CC = 0.15), or Quest (CC = 0.17).

Conclusions: A testosterone RIA is comparable to LC/MS assays. There is significant variability between LC/MS assays and poor precision with all assays at low testosterone levels.

Materials and method

A literature search was performed using electronic databases such as Pubmed/Medline to identify relevant articles using relevant search terms for hypothyroidism, menstrual irregularities, PCOS, infertility, miscarriages and reproductive age group. From this search, publications that met the following criteria-original contributions of hypothyroidism with menstrual irregularities, PCOS, infertility and miscarriages, prospective observational studies, hospital based cross sectional study, along with the review articles, and reports limited to clinical human data that were published in the English language were included in the review. Case reports and case series were not included in the review. All articles considered were published in the scientific literature. Full text articles of relevant abstracts were assessed and evaluated. The search yielded around 18 original studies (hospital based cross sectional study and prospective observational) evaluating association of PCOS with menstrual irregularities infertility and miscarriages which were reviewed and are included in the subsequent sections below.

Polycystic ovary syndrome (PCOS) and LH, FSH and Hypothyroidism

LH and FSH are the hormones that encourage ovulation. Both LH and FSH are secreted by the pituitary gland in the brain. At the beginning of the cycle, LH and FSH levels usually range between about 5-20 mlU/ml. Most women have about equal amounts of LH and FSH during the early part of their cycle. However, there is a LH surge in which the amount of LH increases to about 25-40 mlU/ml 24 hours before ovulation occurs. Once the egg is released by the ovary, the LH levels goes back down. While many women with PCOS still have LH and FSH still within the 5-20 mlU/ml range, their LH level is often two or three times that of the FSH level. For example, it is typical for women with PCOS to have an LH level of about 18 mlU/ml and a FSH level of about 6 mlU/ml (notice that both levels fall within the normal range of 5-20 mlU/ml). This situation is called an elevated LH to FSH ratio or a ratio of 3:1. This change in the LH to FSH ratio is enough to disrupt ovulation. While this used to be considered an important aspect in diagnosing PCOS, it is now considered less useful in diagnosing PCOS, but is still helpful when looking at the overall picture.

Hypothyroidism

Comparison 2–4% of reproductive age group and has been shown to be the cause of infertility and habitual abortion. Moreover, hypothyroidism can initiate, maintain or worsen PCOS. Hence, many studies are done from various parts of the world regarding thyroid disorders in PCOS patient. They have tried to explore the PCOS and thyroid co-relation. Mostly, the results showed higher incidence of elevated Thyroid Stimulating Hormone (TSH) levels and four times higher prevalence of autoimmune thyroiditis in PCOS patients. Again, it is also evident from different study that routine screening for thyroid dysfunction in hyper androgenic patient is of little value since the incidence of these disorders is not higher in hyper androgenic patients than in normal women of child bearing age.

Polycystic ovary syndrome (PCOS) and Estrogen

Estrogen is the female hormone that is secreted mainly by the ovaries and in small quantities by the adrenal glands. The most active estrogen in the body is called estradiol. A sufficient amount of estrogen is needed to work with progesterone to promote menstruation. Most women with PCOS are surprised to find that their estrogen levels fall within the normal range (about 25-75 pg/ml). This may be due to the fact that the high levels of insulin and testosterone found in women with PCOS are sometimes converted to estrogen.

Polycystic ovary syndrome (PCOS) and THS

TSH stands for Thyroid Stimulating Hormone and is produced by the thyroid, a gland found in the neck. Women with PCOS usually have normal TSH levels (0.4-3.8 uIU/ml). TSH is checked to rule out other problems, such as an underactive or overactive thyroid, which often cause irregular or lack of periods and anovulation.

Insulin and Glucose

Due to the recent research that PCOS is probably caused by insulin resistance, physicians are beginning to check glucose levels as a factor when diagnosing PCOS. Most women with polycystic ovary syndrome should have a Fasting Plasma Glucose Test and a Glucose Tolerance Test at diagnosis and periodically thereafter, depending on risk factors. A high glucose level can indicate insulin resistance, a diabetes-related condition that contributes to PCOS.

Cholesterol

Researchers are also beginning to notice a connection between PCOS and heart disease; therefore, some physicians may want to look at your cholesterol levels when diagnosing and treating PCOS. Women with PCOS have a greater tendency to have high cholesterol, a major risk factor for developing heart disease. Cholesterol is a fat-like substance normally used by the body for form cell membranes and certain hormones. A high cholesterol level is considered greater than 200. Also, since the levels of good (high-density lipoproteins or HDL) and bad (low-density lipoproteins or LDL) are sometimes more indicative of a woman's risk for developing heart disease, these levels might also be assessed.

Too much bad cholesterol tends to increase the risk for plaque to build up in the arteries which can lead to a heart attack. Too much good cholesterol is believed to remove the cholesterol from building up in the arteries. Women with PCOS tend to have less good cholesterol and more bad cholesterol. In addition, triglyceride levels, another component of cholesterol, tend to be high in women with PCOS which further contributes to the risk of heart disease. Even if your physician does not check your cholesterol levels when diagnosing PCOS, it is a good idea to have these levels checked periodically since women with PCOS have a greater chance of developing high cholesterol which can lead to heart disease.

Progesterone

Progesterone is produced by the corpus luteum after ovulation occurs. Progesterone helps to prepare the uterine lining for pregnancy. For women with PCOS, especially those who are trying to become pregnant using fertility medications, Progesterone levels are checked about 7 days after it is thought that ovulation occurred. If the Progesterone level is high (usually greater than 14 ng/ml) this means that ovulation did indeed occur and the egg was released from the ovary. If the progesterone level is low the egg was probably not released. This test is especially important because sometimes women with PCOS can have some signs that ovulation is occurring however, when the progesterone test is done, it shows that ovulation did not occur. If this happens, your body is may be producing a follicle and preparing you to ovulate, but for some reason the egg is not actually being released from the ovary. This information helps your physician possibly adjust fertility medication for the next cycle to encourage the release of the egg.

Testosterone

All women have testosterone in their bodies. There are two methods to measure testosterone levels:

- Total Testosterone
- Free Testosterone

Total testosterone refers to the total amount of all testosterone, including the free testosterone, in your body. The range for this is 6.0-86 ng/dl. Free testosterone refers to the amount of testosterone that is unbound and actually active in your body. This amount usually ranges from 0.7-3.6 pg/ml. Women with PCOS often have an increased level of both total testosterone and free testosterone. Furthermore, even a slight increase in testosterone in a woman's body can suppress normal menstruation and ovulation.

DHEA-S

DHEA-S or dehydroepiandrosterone is another male hormone that is found in all women. DHEA-S is an androgen that is secreted by the adrenal gland. It is normal for women to have DHEA-S levels anywhere between 35-430 ug/dl. Most women with PCOS tend to have DHEA-S levels greater than 200 ug/dl.

Prolactin

Prolactin is a pituitary hormone that stimulates and sustains milk production in nursing mothers. Prolactin levels are usually normal in women with PCOS, generally less than 25 ng/ml. However, it is important to check for high prolactin levels in order to rule out other problems, such as a pituitary tumor, that might be causing PCOS-related symptoms. Some women with PCOS do have elevated prolactin levels, typically falling within the 25-40 ng/ml range.

Androstenedione (ANDRO)

ANDRO is a hormone that is produced by the ovaries and adrenal glands. Sometimes high levels of this hormone can affect estrogen and testosterone levels. Normal ANDRO levels are between 0.7 3.1 ng/ml.

Treatment

PCOS treatment focuses on managing your individual concerns, such as infertility, hirsutism, acne or obesity. Specific treatment might involve lifestyle changes or medication.

Lifestyle changes

Your doctor may recommend weight loss through a low-calorie diet combined with moderate exercise activities. Even a modest reduction in your weight — for example, losing 5 percent of your body weight — might improve your condition. Losing weight may also increase the effectiveness of medications your doctor recommends for PCOS, and can help with infertility.

Medications

To regulate your menstrual cycle, your doctor might recommend:

- **Combination birth control pills.** Pills that contain estrogen and progestin decrease androgen production and regulate estrogen. Regulating your hormones can lower your risk of endometrial cancer and correct abnormal bleeding, excess hair growth and acne. Instead of pills, you might use a skin patch or vaginal ring that contains a combination of estrogen and progestin.

- **Progestin therapy.** Taking progestin for 10 to 14 days every one to two months can regulate your periods and protect against endometrial cancer. Progestin therapy doesn't improve androgen levels and won't prevent pregnancy. The progestin-only minipill or progestin-containing intrauterine device is a better choice if you also wish to avoid pregnancy.

To help you ovulate, your doctor might recommend:

- **Clomiphene.** This oral anti-estrogen medication is taken during the first part of your menstrual cycle.

- **Letrozole (Femara).** This breast cancer treatment can work to stimulate the ovaries.

- **Metformin.** This oral medication for type 2 diabetes improves insulin resistance and lowers insulin levels. If you don't become pregnant using clomiphene, your doctor might recommend adding metformin. If you have prediabetes, metformin can also slow the progression to type 2 diabetes and help with weight loss.

- **Gonadotropins.** These hormone medications are given by injection.

To reduce excessive hair growth, your doctor might recommend:

- **Birth control pills.** These pills decrease androgen production that can cause excessive hair growth.

- **Spironolactone (Aldactone).** This medication blocks the effects of androgen on the skin. Spironolactone can cause birth defects, so effective contraception is required while taking this medication. It isn't recommended if you're pregnant or planning to become pregnant.

- **Eflornithine (Vaniqa).** This cream can slow facial hair growth in women.

- **Electrolysis.** A tiny needle is inserted into each hair follicle. The needle emits a pulse of electric current to damage and eventually destroy the follicle. You might need multiple treatments.

To help decrease the effects of PCOS, try to:

- **Maintain a healthy weight.** Weight loss can reduce insulin and androgen levels and may restore ovulation. Ask your doctor about a weight-control program, and meet regularly with a dietitian for help in reaching weight-loss goals.

- **Limit carbohydrates.** Low-fat, high-carbohydrate diets might increase insulin levels. Ask your doctor about a low-carbohydrate diet if you have PCOS. Choose complex carbohydrates, which raise your blood sugar levels more slowly.

- **Be active.** Exercise helps lower blood sugar levels. If you have PCOS, increasing your daily activity and participating in a regular exercise program may treat or even prevent insulin resistance and help you keep your weight under control and avoid developing diabetes.

Conclusion:

PCOS is not just an endocrine disorder, but a combination of metabolic and psychosocial detriments. Not addressing all the aspects of PCOS, such as depression, may delay the treatment of the "primary" issues such as fertility and hyperandrogenism. While further research needs to be conducted with larger sample sizes, current research does suggest a decreased quality of life in this population. It is evident that a universally accepted diagnostic criterion needs to be implemented by researchers and health care professionals. The longer proper treatment is delayed, chances are increased of the patient developing other health issues such as metabolic syndrome and cardiovascular disease. Treating the patient holistically seems like a very simple answer to a large problem; this will only happen if health care professionals are committed to increasing patient education, and helping patients find the proper treatment for all aspects of this disease.

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