



A REVIEW: BRIEF INSIGHT INTO POLYCYSTIC OVARY SYNDROME (PCOS)

Author:

¹Ashwini Ravindra Karale*, ¹Adity College of Pharmacy, Beed, India.

Correspondence author: ¹Ashwini Ravindra Karale

Co-author: ²L.D. Hingane sir.

Abstract

Polycystic ovary syndrome (PCOS) is a chronic, complex and the most common endocrine disorder observed in women of reproductive age. This disease can be diagnosed on the basis of various criteria. This syndrome is heterogeneous by nature. It is a significant public health issue. Due to PCOS patient faces lots of consequence that are Metabolic/Obesity, Reproductive/obstetric, Quality of Life and Behavioural/emotional. PCOS can be screened by lots by methods. This disease cause by hormonal imbalance. In patient, lots of symptoms occur due to PCOS. It affects physically and psychologically. Prevalence is quite high and it is increasing day by day. It is a syndrome to be prevented by awakening awareness in health workers and patients. There are many areas of controversies starting from its diagnosis, pathogenesis, consequences and treatment The European Society for Human Reproduction and Embryology (ESHRE) and the American Society of Reproductive Medicine jointly sponsored a multi-year international evidence-based guideline development process for the International PCOS network, which is made up of geographically diverse international PCOS experts as well as consumers (ASRM).

Keywords: Polycystic ovary syndrome; PCOS; Treatment, Screening of PCOS, New technology.

I. Introduction:

Stein and Leventhal, who noted a syndrome in women marked by irregular menstruation, obesity, and hirsutism in addition to cysts on the women's ovaries, made the first official diagnosis of this endocrine ailment in 1935. (8) If other specific diseases have been ruled out, such as hyperprolactinemia and non-classical congenital adrenal hyperplasia, as well as polycystic ovarian morphology, then polycystic ovary syndrome (PCOS) is characterised by a combination of hirsutism, hyperandrogenism, and/or oligo-ovulation as indications of ovarian malfunction (PCOM). (1) Regrettably, unlike the scientific community, the pharmaceutical industry and, in particular, the national and municipal health authorities, have not demonstrated the same level of interest in PCOS. Stein and Leventhal introduced PCOS for the first time in 1935. (1) That is a serious matter for the public's health. Yet, managing these traits is only one aspect of PCOS's health hazards, which likely endure through menopause and beyond the reproductive years.(5) Women present with a variety of characteristics, including reproductive (complications during pregnancy, irregular menstrual cycles, hirsutism, infertility, and anxiety), psychosocial (anxiety, depression, body image, and reduced quality of life)8, and major metabolic abnormalities (insulin resistance, metabolic syndrome, prediabetes, type 2 diabetes mellitus and cardiovascular risk factors). (9), increasing the severity of the disorder, causing great concern for people affected, and requiring attention to healthy lifestyle. There is also an increased rate of weight gain and prevalence of obesity in PCOS. (10) PCOS has the potential to have negative effects that could be life-altering, such as a higher risk of endometrial hyperplasia and neoplasia. (2) That is a serious matter for the public's health. Yet, managing these traits is only one aspect of PCOS's health hazards, which likely endure through menopause and beyond the reproductive years. (5) Women exhibit a variety of characteristics, such as substantial metabolic aspects, irregular menstrual cycles, hirsutism,

infertility, and psychosocial (anxiety, depression, body image, and decreased quality of life) traits (insulin resistance, metabolic syndrome, prediabetes, type 2 diabetes mellitus and cardiovascular risk factors). (2)

II. The term 'polycystic ovary syndrome'

That is a significant issue for the general public's health. Yet, controlling these characteristics is just one component of PCOS's health risks, which are likely to last through menopause and the reproductive years. (5) Women display a range of traits, including significant metabolic differences, irregular menstrual cycles, hirsutism, infertility, and psychosocial abnormalities (such as anxiety, sadness, body image issues, and a poor quality of life) (insulin resistance, metabolic syndrome, prediabetes, type 2 diabetes mellitus and cardiovascular risk factors). (2). Ovarian follicles are cellular clusters that each contain a single oocyte; they are not cysts, which are membrane sacs or cavities with aberrant characteristics that hold fluid; as a result, the term PCOS may be misleading. Unfortunately, this misconception obscures the pathogenesis of the disease (16). Primary healthcare providers and patients both find the name PCOS to be misleading, and it's not uncommon for patients and their families to voice irrational concerns about the potential for malignancy of such "cysts". Hence, a new nomenclature for PCOS was suggested at the 2012 National Institutes of Health Office for Disease Prevention-Sponsored Evidence-Based Methodological Workshop on Polycystic Ovary Syndrome. A PCOS patient support group from Australia and a few professional associations all firmly backed this suggestion in an effort to ensure that "...an alternative term promotes comprehension and awareness of the disease and its complicated aspects." (1)

III. Definition of PCOS

Although the 2012 Evidence-Based Methodology Workshop on Polycystic Ovary Syndrome, aimed to put an end to the discussion regarding the best diagnostic standards for PCOS, the steering committee's report was not published in a peer-reviewed scientific journal, which diminished its authority and impact. Therefore, the recommendation to use the so-called Rotterdam criteria, which were jointly proposed in 2003 by members of the European Society of Human Reproduction and Embryology and the American Society of Reproductive Medicine, has not gained widespread acceptance. Three definitions of PCOS are still in use today.

The most prevalent endocrine issue seen in women of reproductive age is polycystic ovarian syndrome (PCOS), which is a chronic, complex condition that also affects teenagers. (1) Up to 70% of the affected women go for a long time without receiving a diagnosis or are diagnosed much later than expected. (2) Depending on the definition and the demographic analysed, the prevalence is typically estimated to be between 6-20%. In the absence of other distinct diagnoses, this condition, which is heterogeneous by nature, is characterised by a combination of signs and symptoms of androgen excess and ovarian dysfunction. (4) Women with PCOS frequently exhibit oligomenorrhea, hirsutism, or infertility symptoms in their youth or early adulthood. (5) Recent research reveals that PCOS is a lifelong syndrome that first manifests during pregnancy, despite the fact that it was traditionally thought to be a disorder that only affected adult women. (6) That is a serious matter for the public's health. Yet, managing these traits is only one aspect of PCOS's health hazards, which likely endure through menopause and beyond the reproductive years. (3)

IV. Aetiology and pathophysiology of PCOS

Due to the complexity of this disorder, several sets of diagnostic criteria have been developed. AMH is a prominent hormonal indication that plays a significant role in the maturation and growth of ovarian follicles in PCOS patients, in addition to the three diagnostic criteria (Broekmans et al., 2008). The follicular growth is hampered by excessive AMH secretion, which causes ovarian dysfunction. (3) Genetic factors also contribute to the aetiology of PCOS, in addition to environmental variables. SNPs and candidate genes are involved in its causation. Databases indicate that 241 gene variants contribute to the pathogenesis of PCOS. A deficiency in a gene's transcriptional activity caused by polymorphism or any nucleotide variation results in PCOS. The majority of the blame is placed on genes that encode for the androgen receptor, luteinizing hormone receptors, follicular stimulating hormone receptors, and leptin receptors. (4) Hereditary factors play a role in polycystic ovaries, elevated androgen levels brought on by defective ovarian cells (likely theca cells), and IR. Congenital or acquired environmental factors that affect phenotypic include intrauterine factors like androgen exposure and prenatal nutrition, especially intrauterine growth restriction. Acquired obesity is a significant postnatal influence. Generally speaking, the intricate interplay between various influencing factors resembles an autosomal dominant trait with varied penetrance. The phenotypic variety and prevalence of the syndrome are also influenced by ethnic diversity. PCOS is more common in Spanish-speaking, Native American, and Mexican women. (2)

V. Environmental factors influencing PCOS

Endocrine disrupting chemicals (EDCs) are defined as "exogenous agents that interfere with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are necessary for the maintenance of homeostasis, reproduction, development, and/or behaviour" by the United States Environmental Protection Agency (USEPA) (5)

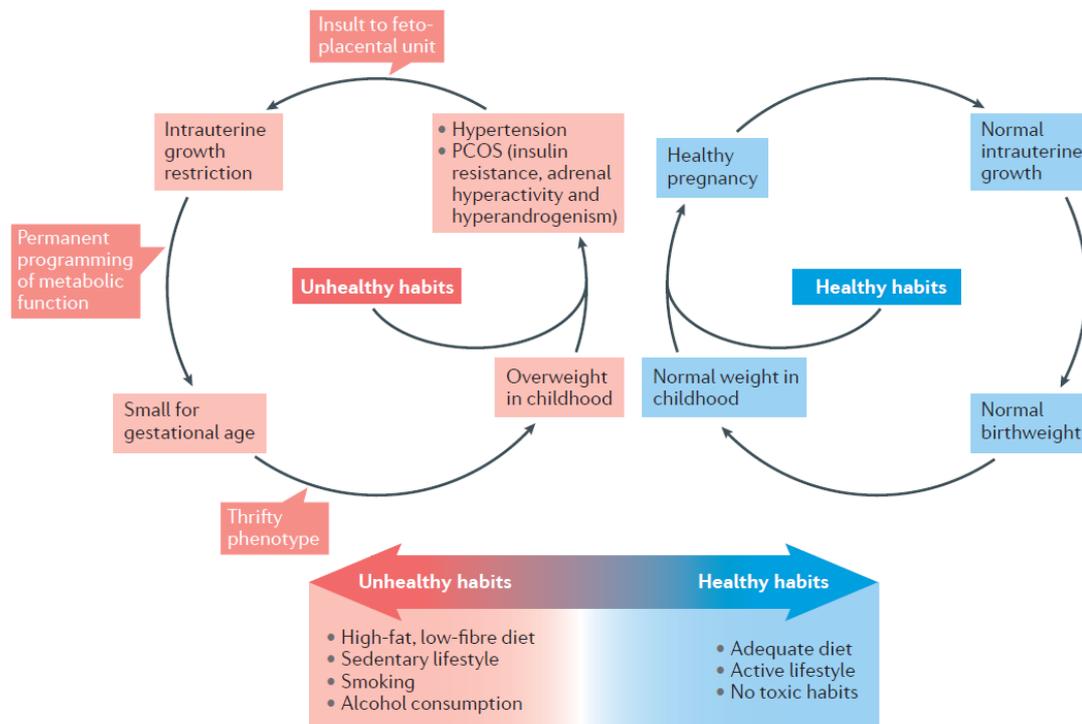


Fig 1

VI. Diagnosis of PCOS

AE-PCOS is for the Androgen Excess and PCOS Society. ASRM stands for the American Society of Reproductive Medicine. Hyperandrogenism (HA), ovarian dysfunction (OD), and polycystic ovarian morphology (PCOM) (12 follicles and 2-9 mm in each ovary). Determining whether a patient has PCOS must be a straightforward process, as the criteria used in all current classifications are the same. (1) After ruling out other related conditions, the National Institutes of Health (NIH) made its initial effort at diagnosis in 1990, using oligo- or anovulation and hyperandrogenism (HA) as the two criteria to identify PCOS. (2) Two of these three criteria—HA, ovulation dysfunction, and PCOM—must be present in order to diagnose PCOS, according to the Rotterdam criteria, which were developed by the Rotterdam ESHRE/ASRM sponsored PCOS Consensus Workshop Group in 2003. PCOM, an ultrasound finding of polycystic ovaries, was added to the NIH criteria. (3)

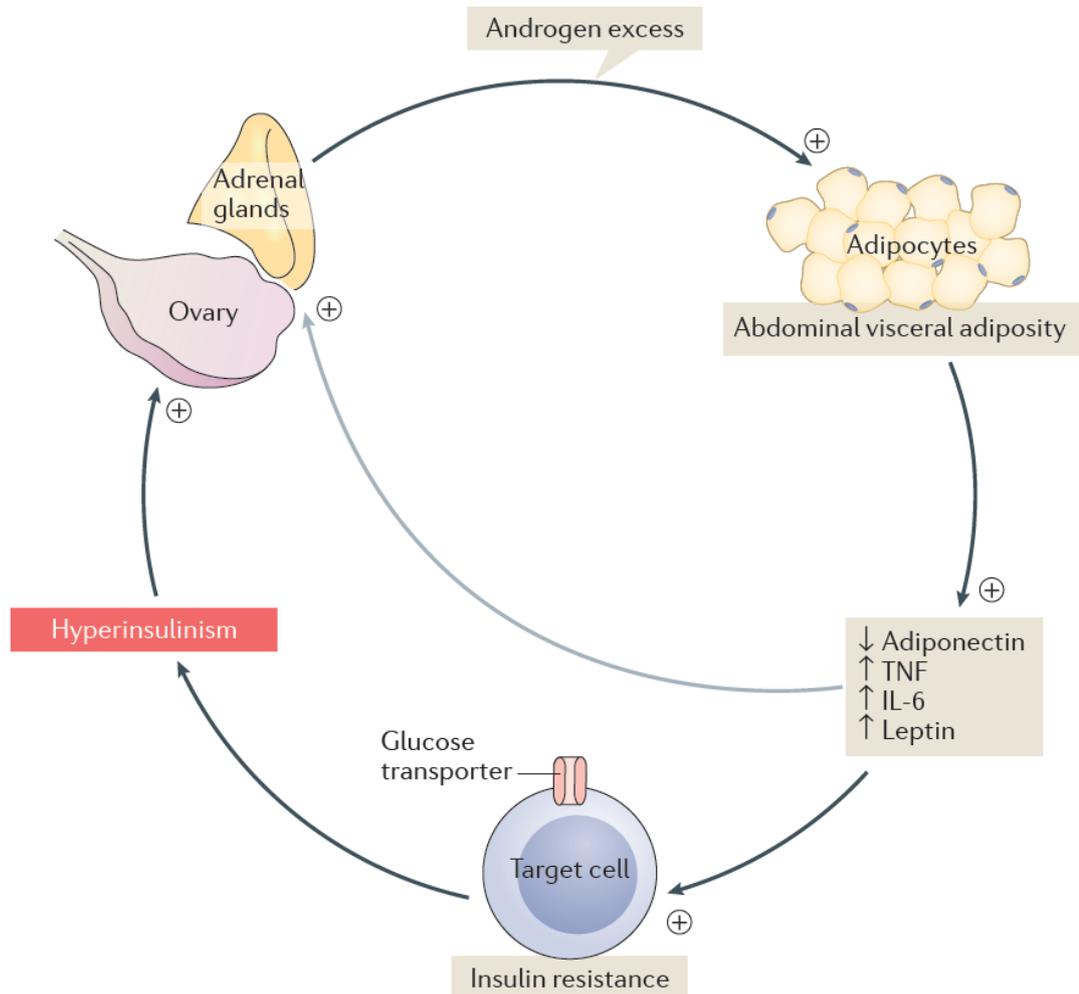


Fig 2.

Adult Diagnostic Criteria (Rotterdam)	
Otherwise, unexplained alternative phenotypes:	
1	Phenotype 1 (Classic PCOS)
	a. Clinical and/or biochemical evidence of hyperandrogenism
	b. Evidence of oligo-anovulation
	c. Ultrasonographic evidence of a polycystic ovary
2	Phenotype 2 (Essential NIH Criteria)
	a. Clinical and/or biochemical evidence of hyperandrogenism
	b. Evidence of oligo-anovulation
3	Phenotype 3 (Ovulatory PCOS)
	a. Clinical and/or biochemical evidence of hyperandrogenism
	b. Ultrasonographic evidence of a polycystic ovary
4	Phenotype 4 (Nonhyperandrogenic PCOS)
	a. Evidence of oligo-anovulation
	b. Ultrasonographic evidence of a polycystic ovary
Adolescent Diagnostic Criteria	
Otherwise, unexplained combination of:	
1	Abnormal uterine bleeding pattern
	a. Abnormal for age or gynecologic age
	b. Persistent symptoms for 1–2 y

2	Evidence of hyperandrogenism
	a. Persistent testosterone elevation above adult norms in a reliable reference laboratory is the best evidence
	b. Moderate-severe hirsutism is clinical evidence of hyperandrogenism

(2)

VII. PCOS symptoms:

The International PCOS guideline established recommendations for managing PCOS-related symptoms essential to diagnosis, notably irregular periods, hirsutism, and anovulation. Medical intervention is only advised as a second-line therapy following lifestyle adjustment because hyperinsulinemia increases hyperandrogenism. In terms of medical interventions, combination contraceptives (COCs) are superior to progestin-only medications for the treatment of hirsutism and acne in addition to being effective in treating irregular periods. Given that there is no evidence to support the superiority of any specific estrogen-progestin combination, the choice of COC can be made based on administration preferences and limiting the adverse effect profile to ensure compliance. 3 Notably, per WHO advice, 35ug oestrogen in conjunction with cyproterone acetate should only be used as a last resort for chronic acne or hirsutism due to the elevated risk for vascular thrombosis associated with these medications.

VIII. Consequences**Metabolic/Obesity:**

From an early age, PCOS is linked to a higher risk of metabolic problems. Among these comorbidities are common risk factors for cardiovascular disease (CVD), such as obesity, impaired glucose tolerance (IGT), type 2 diabetes (DM), dyslipidemia, and hypertension. One of the top concerns raised by PCOS patients in surveys is obesity. The obesity rate ranges from 50 to 80 percent depending on the research group and ethnicity examined. The risk of obesity in women with PCOS was shown to be four times higher compared to controls and higher in white women compared to Asian women after reviewing high quality research in a significant meta-analysis. It is significant to note that women with PCOS have been proven to have long-term obesity or overweight, with the start of the BMI trajectory deviation happening as early as age 5. Data from cross-sectional research indicates that the risk of being overweight or obese continues through the fourth decade of life, and a few longitudinal studies also point to an increase in weight with advancing age. (6) The limited research done on teenagers and older women do not reveal any notable variations from control groups. The significance of mild to moderately aberrant findings for blood pressure measures and serum lipids over the long term is unclear because the majority of the information on metabolic risk is generated from cross-sectional studies. Another strategy is to examine the prevalence of metabolic syndrome, which calculates a composite score from early signs of hypertension, dyslipidaemia, glucose intolerance, and obesity and may indicate long-term risk of DM and CVD. With a higher risk in the hyperandrogenic phenotype, metabolic syndrome is two times more likely in reproductive-age women with PCOS. (6)

Reproductive/obstetric:

Endometrial hyperplasia and infertility caused by anovulation are more common in PCOS-afflicted women. The risk of endometrial cancer in premenopausal women with PCOS may be four times higher. Letrozole, an ovulation inducer, has greater live birth rates than clomiphene citrate when used by PCOS-afflicted women who are trying to conceive. In a subpopulation of obese women, taking metformin in addition to these drugs may increase the ovulation rate. The obesity rate ranges from 50 to 80 percent, depending on the ethnic group and research population examined (e.g., clinical cohorts vs. community-based studies). Contrarily, metformin has not been demonstrated to lower the risk of gestational diabetes (GDM); as a result, its usage should be restricted to before pregnancy for metabolic management and to promote weight loss. Women with PCOS have a higher risk of miscarriage, GDM, pregnancy-induced hypertension, and preeclampsia once they become pregnant. The hyperandrogenic phenotypes are more likely to have these problems.

Behavioral/emotional:

Psychiatric illnesses are more common in people with PCOS. Cross-sectional studies show an increase in moderate to severe depressed and anxiety symptoms, whereas a few longitudinal studies show an increased risk of incident depression and anxiety. Although current research suggests psychological distress persisting over a lengthy period of time, there is little information on the persistence of depression and anxiety symptoms in teens and beyond the fourth decade. Moreover, compulsive eating and concern about body image are more common among PCOS-positive women. It's interesting to note that in the latter trial, different parts of body image distress predicted anxiety and depressed scores, suggesting that a positive change in body image can lessen anxiety and depressive symptoms. demonstrating that a more positive body image may help to lessen anxiety and depression symptoms. The difficulty of losing weight is exacerbated by both eating disorders and negative body image, emphasising the significance of frequent screening for these illnesses and the use of therapies such cognitive behavioural therapy. (6)

Quality of Life:

Women with PCOS struggle with comorbid conditions and symptoms. Health practitioners and women should be aware of the negative effects of PCOS on health-related quality of life (QoL), which seem to persist at least into the late reproductive years. Women with PCOS report having worse health status than their non-PCOS counterparts. (6)

IX. Physical examination:

Histological examination of ovaries from women with PCOS has shown that there is a doubling of the cross-sectional area, doubling of the number of ripening and atretic follicles, a 50% increase in the thickness of the tunica, a 33% increase in cortical stromal thickness and a 5-fold increase in the subcortical (medulla) stroma (Hughesdon, 1982). (7)

Ultrasound imaging:

PCO has also been associated with a decreased uterine width to ovarian length ratio of larger than 1.0.

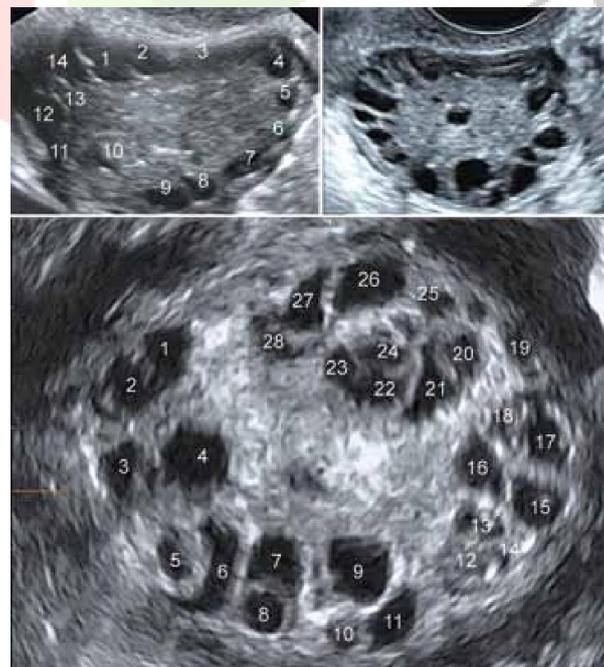


Fig 3. Transvaginal 2D scan using a 7.5 MHz probe in a PCOS patient: antral follicles are measured and numbered in this image in two different spatial planes.

3D ultrasound:

Using a volumetric probe or performing a manual examination of the ovary, 3D ultrasonography has been suggested as a solution to the challenges associated with defining or measuring ovarian size (16)

Transvaginal colour flow imaging of the uterine arteries during the ovarian and menstrual cycles:

Using an endovaginally probe that produced a 6.0 MHz pulsed colour Doppler system for blood flow analysis and a 7.5 MHz pulsed beam for imaging, a Sonotron Vingmed CFM 700 scanner (Diasonics Sonotron Ltd, Bedford, UK) was employed. The relationship between the Doppler frequency shift and the colour intensity was linear. Blood flow towards or away from the probe was depicted by the colours red and blue, respectively. The maximum limit for use in foetal medicine set by the Bioeffects Committee of the American Institute of Ultrasound in Medicine (Gill, 1982) was well within the spatial peak temporal average intensity for all ultrasonic components of the probe, which was -65 mW/cm^2 . (18)

MRI

Pelvic MRI in our overweight and obese virginal adolescent girls systematically. Abdominal US failure was mainly due to limitations in available US probes to allow better definition of ovarian structures, as this was hampered by excess subcutaneous abdominal fat. In our study population, the mean volumes of the right and left ovaries were 1.96 SDS ml and 13.66 1.26 SDS ml, respectively. T2-weighted clearly showed the dispersion of the follicles and their peripheral placement. Follicles per ovary were greater than 12 (22.0 versus 10.0 in Cappa et al. normal's control; Z, 2.12, P 0.05). The follicular volume could not, regrettably, be measured. Overall, pelvic MRI improved the definition of ovarian morphology and provided a good picture of the follicles' distribution in the periphery as well as the enlarged stromal components that are typical of PCOS. (19)

Screening for Type 2 DM and GDM

All obese PCOS women and lean PCOS patients older than 40 with a history of GDM or a family history of T2DM are advised to undergo an oral glucose tolerance test (OGTT), according to the European Society of Endocrinology (ESE). On the other hand, because PCOS patients have a higher-than-average risk of developing IGT and T2DM, the Endocrine Society and ESHRE/ASRM advise performing OGTT in all teenage and adult PCOS patients. Hemoglobin A1c (HbA1c) as a screening test is not advised by either of the organisations. The screening should be performed every three to five years, or every two years in individuals without type 2 DM risk factors and once a year in those with risk factors. A recent worldwide guideline for PCOS advises an OGTT prior to conception or throughout the first 24 to 28 weeks of pregnancy. (2)

Screening for Psychological Wellbeing

Potential risk factors for psychological problems should be examined in women with PCOS at the time of diagnosis. Recommendations advise screening these women for poor body image, eating disorders, and psychosexual dysfunction in addition to sadness and anxiety. If the screening results are favourable, a doctor's evaluation is continued and a specialist referral is advised. Teenagers should be screened because some studies show an increased incidence of depression in this age range. (2)

X. Study on PCOS

Many studies have found a genetic connection; nevertheless, the manner of inheritance is still unknown, and there is no consensus on how it works (Franks et al., 2006). The most likely causes are oligogenic or polygenic, which, respectively, refer to a genetic trait created by one or only a few genes, or by multiple genes ("Medical Dictionary," 2013). It is possible that the reason is an autosomal dominant mechanism, several genes, or both (Franks et al., 2006) According to the Medical Dictionary's 2013 edition, an autosomal dominant method of inheritance describes a characteristic that is inherited without regard to sex and does not involve a sex chromosome. (8)

XI. THE ROLE OF NEW TECHNOLOGY:

It is now possible to assess the ovary's volume and area using sophisticated modern computerised US equipment, which may present a valuable opportunity for completely objective comparative studies of normal and polycystic ovaries. Comparably, the development of transvaginal colour Doppler ultrasound may advance our understanding of the ovarian hemodynamic alterations and provide important information about potential pathogenic processes for PCOS (Battaglia et al, 1995; Zaidi et al, 1995). (17)

XII. Hormonal association with PCOS:

A study that looked at the relationship between PCOS and hormone levels in the Pakistani population. Both impacted and healthy people are included in this cross-sectional investigation. Blood was obtained for hormonal measurement using immunoradiometric test and radioimmunoassay, and a clinical examination was documented. They came to the conclusion that PCOS patients had significantly higher levels of BMI, FSH, LH, and prolactin than healthy people did. FSH, LH, and androgen level are the fundamental variables that must be taken into account for the diagnosis of PCOS. An increase in androgen due to elevated LH levels causes PCOS to proceed. (9)

XIII. Genetic predisposition & PCOS:

A high genetic link exists for PCOS. Discussed genes include CAPN10, Cytochrome family p450, Insulin gene, AR, FTO, and FSHR. (9)

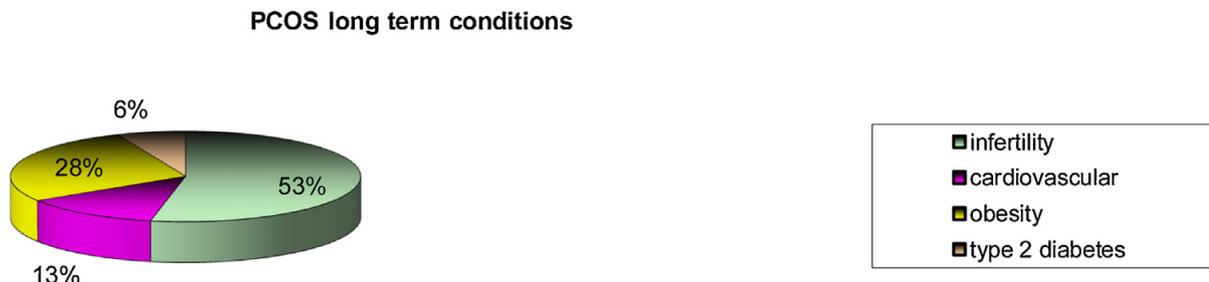
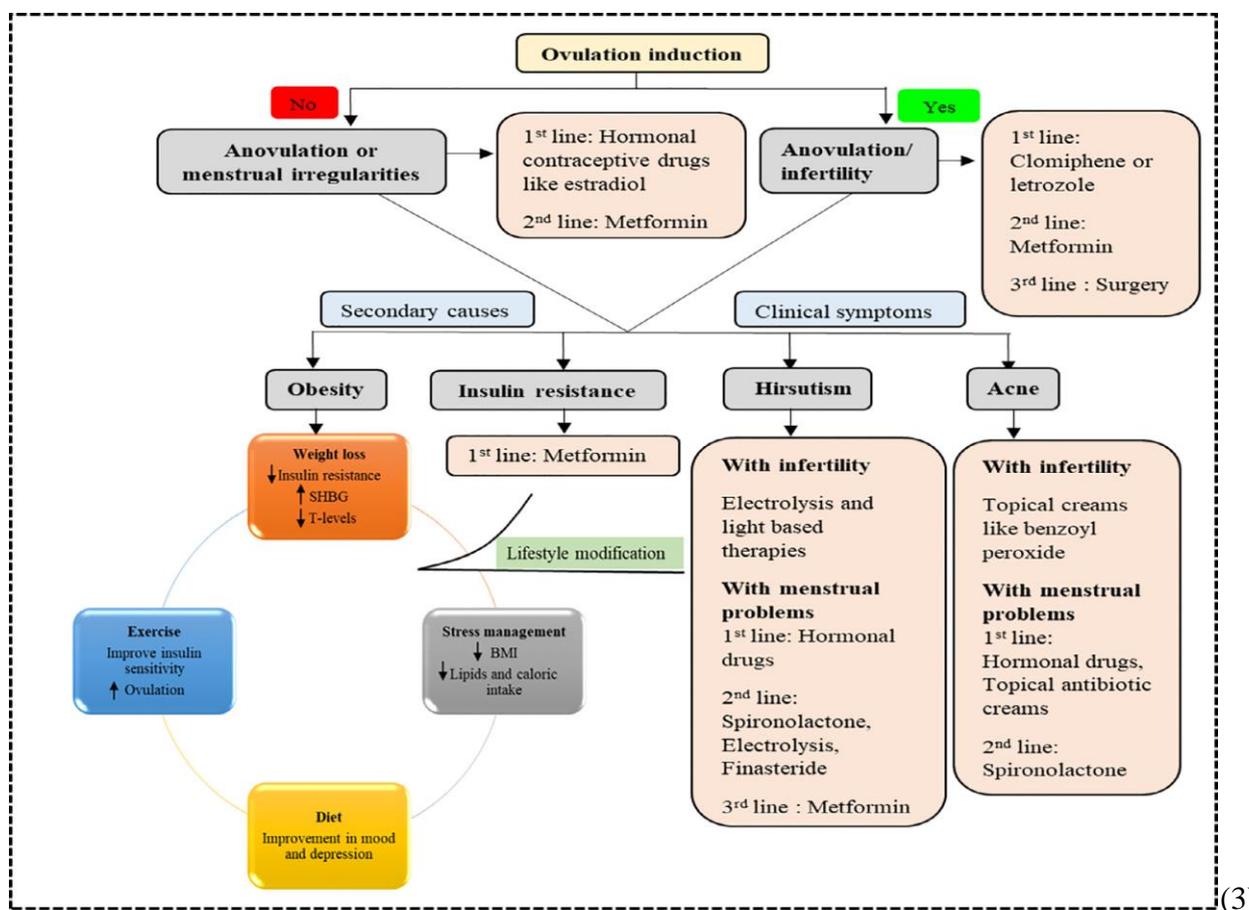


Fig. 4. PCOS long term condition. (9)

XIV. Treatment:

Principles of the treatment of PCOS: (1)

- No universal treatment for PCOS exists.
- Treatment is symptom-oriented.
- Other than lifestyle recommendations, patients with mild symptoms might not require any intervention.
- No drugs are currently approved specifically for PCOS.
- Targets for pharmacological treatment should consider androgen excess, oligo-ovulation and insulin resistance.
- Treatment should be chronic and dynamic and adapted to the changing circumstances, personal needs and expectations of the individual patient.



(3)

Fig 5: Polycystic ovary management protocol stating the treatment options for anovulation and infertility including clinical symptoms.

XV. Conclusions:

In order to allay concerns raised by both physicians and patients over diagnostic delay, clear diagnostic protocols should enable more quick and accurate diagnosis. PCOS pathogenesis is intricate and complicated. With PCOS, comorbidities are widely reported, and it is crucial to assess and treat these comorbidities early in the treatment course, paying special emphasis to mental health and quality of life indicators. The function of PCOS in cardiovascular disease is still unknown, despite the fact that metabolic abnormalities are well-described. (6) Measuring testosterone alone is the most sensitive biochemical indicator of PCOS, but combining it with androstenedione and LH raised sensitivity to 86%. While pelvic ultrasound examination results show typical appearances, it is best to base the diagnosis of polycystic ovarian syndrome on clinical signs. Hormone testing may further support the diagnosis. (15)

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