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Critical Review Of Polycystic Ovarian Syndrome

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Abstract

Polycystic Ovarian Syndrome, which was originally described by Stein and Leventhal, is complex, multifactorial and polygenic manifestation. Globally around 11-13% of women are battling with this condition. It mainly hampers the reproductive health of women leading infertility. Since 1990, many clinical and biochemical criteria and guidelines has been established for the diagnosis of PCOS. Multiple theories and metabolic pathways are introduced while understanding its pathophysiology. It comprises of hyperandrogenism, anovulation, multiple immature follicles. Dysregulation of genes and upregulation of enzymes in androgen synthesis also contribute to this endocrine disorder. It is often associated with Insulin resistance, obesity, and genetic factors. Chronicity of the disease may lead to cardiovascular diseases, diabetes type 2, endometrial cancer. Exact etiology remains unclear but environmental, genetic, lifestyle modifications are thought contribute to its development. Treatment includes hormonal therapies i.e. Combined oral pills, bigunides, fertility medications i.e. Ovulation inductors, aromatase inhibitors and surgical interventions. Beside lifestyle modification and weight management, understanding of Insulin resistance is a crucial key in its treatment. Early diagnosis and management can help to improve quality of reproductive health. In this review article all the guidelines, etiology, pathophysiology, signs and symptoms, investigations, short and long term consequences and management have been detailed. Further research is needed to understand its underlying cause and effective prevention and treatment strategies. A multidisciplinary approach, involving researchers, patients and healthcare provider is essential for improving outcomes and reproductive health. Additional, awareness should be increased in order to reduce stigma and improve diagnosis

Keywords: Polygenic, Multifactorial, Pathophysiology, Hyperandrogenism, Infertility, Endocrine.

Aims and Objectives: To conduct a comprehensive review of PCOS, synthesizing current knowledge on its pathophysiology, diagnosis and management.

Objectives:

- Summarize the epidemiology and prevalence of PCOS.
- Examine genetic, environmental and hormonal factors contributing to PCOS.
- Evaluate diagnostic criteria and biomarkers.
- Discuss treatment options, including pharmacological and lifestyle interventions.
- Assess the impact of the disease on mental health, fertility and metabolic outcomes.
- Provide evidence-based recommendations for healthcare providers and patients
- Enhance understanding and management of PCOS.

Data sources:

- Electronic database – PubMed, Web of Science
- Published peer reviewed articles
- Literature searches
- Medical journals-Journal of endocrinology, fertility
- Textbooks of endocrinology
- Textbooks of gynecology
- Information is collected from secondary data

Introduction

Polycystic Ovarian Syndrome is Cluster of multiple pathophysilogies and pathways. It is characterized by hormonal imbalance, insulin resistance and ovarian dysfunction. PCOS presents with wide range of symptoms, including menstrual abnormalities, hyperandrogenism and polycystic ovaries. The syndrome is leading cause of infertility and women with PCOS, are at increased risk of developing metabolic and cardiovascular diseases, such as type 2 diabetes, hypertension, dyslipidemia. Hormonal treatment, psychological support, lifestyle changes are essential for management of this syndrome.

Factors involved in PCOS-

1.LH 5. Insulin 9. Dehydroepiandrosterone

2.FSH 6. Androgen 10. SHBG

3.TSH 7. Estrogen 11. Testosterone

4.AMH 8. Progesterone

Pathophysiology:

1. Hypothalamo pituitary ovarian compartment abnormality.
2. Androgen excess and hirsutism
3. Obesity and insulin resistance

A] Pathophysiology 1:

GnRH pulse frequency increases.
⇩
GnRH is prefertial to LH rather than FSH.
⇩
C] LH:FSH ratio increases
⇩
LH receptors are present in theca cells.
⇩
As LH increases, theca cells produce more androgen.
⇩
Androgen diffuses through granulosa cells where it gets aromatized and converted into estrogen.

B] Pathophysiology 2:

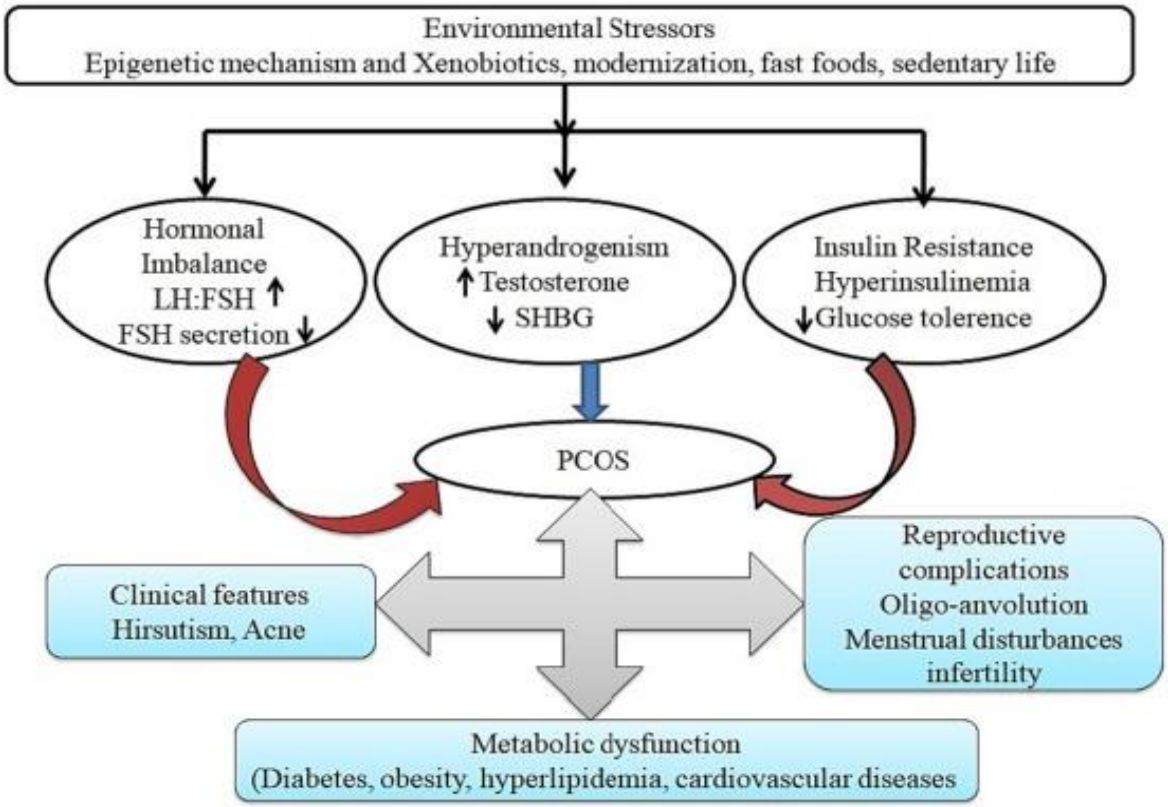
Hyperinsulinemia
⇩
Acts on liver
⇩
Sex Hormone Binding Globulin reduced
⇩
Free androgen in blood stream
⇩
Hyperandrogenism

C] Pathophysiology 3:

FSH **decreases** compared to LH
⇩
Follicular maturation process regression
⇩
Multiple follicle growth arrested
⇩
Antral and preantral follicles produce AMH and more androgen produced due to increase LH
⇩
AMH rises and the ovarian environment becomes androgenic.

D] Pathophysiology 4:

In obese person adipose tissues are more
⇩
Aromatization of androgen in estrogen in adipose tissues



Diagnostic criteria for PCOS:

PCOS diagnostic criteria –

1. 2003 – European society for Human Reproduction and Embryology (ESHRE) and American Society For Reproductive Medicine (ASRM) in Rotterdam Conference.
   Any 2 of 3 criteria –
   A. Oligo / Anovulation.
   B. Clinical or Biochemical hyperandrogenism
   C. Polycystic ovaries

Revised (ESHRE) scales – 15th august 2023

- FNPO – Follicular number per ovary>20 on general usg or > 10 in cross section
- The volume of the ovary >10 ml in only 1 ovary is sufficient for diagnostic criteria.

Clinical features:

1.Oligo/ Anovulation

2.[Hyperandrogenism]hirsutism

3. Menstrual abnormalities

4. Acne

5. Acanthosis nigricans

HAIRAN syndrome – Hyperandrogenism, Insulin Resistance and Acanthosis nigricans

Investigations -

1.LH - Normal range – a. Follicular phase -1.68-15IU/L

b. Ovulatory peak- 21.9-56.6IU/L

c. Luteal phase – 0.61-16.3IU/L

d. Post menopausal- 14.2 -52.3 IU/L

2.FSH Normal range- a. Folllicular phase – 1.4-9.9mIU/mL

b. Ovulatory peak – 6.2-17.2 Miu/mL

c. Luteal phase- 1.1-9.2Miu/Ml

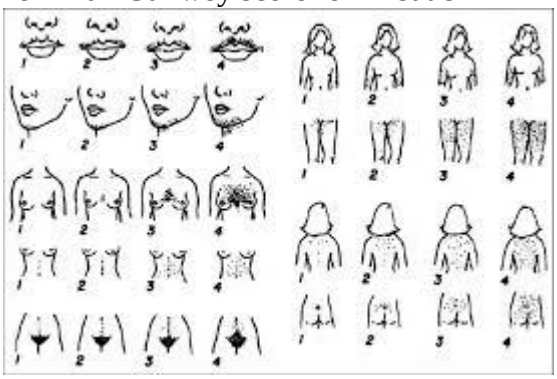
- Serum testosterone
- DHEA
- AMH
- TSH
- USG abdominal or transvaginal
- BSL fasting [70-125mg/dl] PP [upto 150mg/dl]
- OGTT and OGCT [150mg/dl]
- Fasting insulin [<25mU/L]
- LDL [<100mg/dl]
- HDL [>50mg/dl]
- HOMA IR
- IGF

1.Metabollic parameters- HOMA IR – $\frac{\text{Insulin Mu/ml} \times \text{glucose mmol/L}}{405}$

2. QUICKI Index - $\frac{1}{\text{Log of glucose mg/dl} + \text{log of insulin Mu/ml}}$

3.Free ANDROGEN Index - $\frac{\text{total testosterone} \times 100}{\text{SHBG}}$

3. Ferriman Gallwey score for hirsutism



Differential diagnosis:

1. Neoplastic growth of ovary or adreal gland
2. Congeital adrenal hyperplasia
3. Cushing's syndrome
4. Syndrome of sever insulin resistance.

Short term sequelae	Long term sequelae
obesity	Diabetes mellitus
Menstrual abnormalities	Endometrial cancer
Insulin resistance	Cardiovascular disease
Hirsuitism	Obstructive sleep apnea
Acne	hypertension

Treatment

⇩

Lifestyle modification and weight management

⇩

Patient willing to conceive — patient not willing to conceive

A] Combined oral contraceptive pills- progesterone suppresses LH and estrogen improves SHBG reducing free testosterone

B] To reduce hirsutism, antiandrogenic are used

C] Metformin in used as an oral insulin sensitizing agent

D] in patients who are willing to conceive, ovulation induction is done.

E] Laparoscopic ovarian drilling is surgical intervention.

- Hormonal contraceptives: It is the first line of treatment for the patients having menstrual dysfunction, hirsutism, acne, Progestin decreases LH levels , indirectly decreasing ovarian androgen production and increasing sex hormone binding globulin.
- Metformin- Endocrine society recommends starting metformin in PCOS patients with DM2 or IGT who fail lifestyle modification. It improves menstrual cycles, abnormal waist to hip ratip and vascular markers in non-obese women with PCOS.
- Clomiphene citrate: it is a nonsteroid triphenylethylene compound. In the hypothalamus, it binds to estrogen receptors. The negative feedback of endogenous estrogen is prevented. The frequency of pulsatile GnRH increases for both LH and FSH.
- Aromatase inhibitor: It inhibits the enzyme aromatase in the granulosa cells of ovarian follicle. Letrozole is commonly used.

- Cyproterone acetate: It is antiandrogenic progesterone. It inhibits gonadotropic secretion and also act as competitive androgen receptor antagonist.
- Spironolactone: It is androgen receptor antagonist. It is anti-aldosterone diuretic. It also inhibits androgen biosynthesis from ovary and adrenal.
- Flutamide: It is non-steroidal androgen receptor antagonist.
- Finasteride- It inhibits 5 alpha reductase activity.

Discussion: It is complex and multifaceted disorder that affects millions of women in the world. The high prevalence of PCOS, combined in association with various comorbidities, emphasizes the need for early diagnosis and effective management. However, the lack of standardized diagnostic criteria and limited understanding of PCOS pathophysiology hinder efforts to develop target treatment. Healthcare providers should be aware of the complex presentation of PCOS and the need for comprehensive diagnosis and management.

Conclusion: As PCOS is majorly lifestyle syndrome, one should follow the practice of weight management, diet and exercise. Even if there is availability multiple drugs, without lifestyle changes cure and prevention is not possible. This review underscores the importance of multidisciplinary approach to PCOS management, incorporating hormonal therapies, fertility treatment, lifestyle modification and weight management. It emphasizes the need for continued research, improved diagnosis and management. It highlights the research on long term health outcomes and effective strategies addressing details of the disease, we can work towards better management of this complex disorder.

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