## OBESITY AND POLYCYSTIC OVARY SYNDROME

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## INTRODUCTION

 Polycystic ovary syndrome (PCOS) is the most common endocrinological disorder affecting 5% to 10% of women of reproductive age.

(Cooney LG and Dokras A, 2018)

 It is crucial to diagnose PCOS early in its course to delay or arrest its metabolic sequelae.

(Samer El Hayek et al., 2016)

## **Definition of PCOS**

• There is no universally accepted definition for PCOS!

(Dewailly 2000)

### **Historical Aspects of PCOS**

• In 1935, Stein and Leventhal described the features of 7 hirsute, amenorrheic women based on the characteristic ovarian morphology from histological specimens taken at wedge resection of the ovaries.

(Azziz R & Adashi EY, 2016)



- Chronic anovulation.
- Cl and/or biochemical hyperandrogenism.



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- Ch anovulation.
- Cl and/or biochemical hyperandrogenism.
- PCO on US



AES ((2006 AE-PCOS((2009

- Cl and/or biochemical hyperandrogenism.
- Ovarian dysfunction )anovulation and/or PCO(

 Exclusion of related ovulatory or other androgen excess disorders )e.g., thyroid dysfunction, hyperprolactinemia, androgen-secreting neoplasms, or non classic adrenal hyperplasia(

#### **Prevalence of PCOS**

8% 18% 12%
NIH: National Institute of Health
ESHRE: European Society of Human Reproduction and
Embryology
AES: Androgen Excess Society
AES: Androgen Excess Society



#### **PCO on ultrasound**

#### Criteria of polycystic ovarian morphology

- 12 or more follicles, 2 9 mm in diameter and/or
- > Ovarian volume >10 cm<sup>3</sup>.





## **PCOS-Epidemiology**

- PCOS accounts for 95% of cases of hyperandrogenism
- PCOS is responsible for:
- ➢ over 20% of all cases of amenorrhea.
- > up to 75% of all cases of anovulatory infertility.

(Susan M & Kristen A, 2014)

#### Four different phenotypes of PCOS based on Rotterdam Criteria

PCOS phenotypes	Oligo or anovulation	Biochemical or clinical manifestations of hyperandrogemia	PCO in TVS
- <sup>1</sup> Severe PCOS (A)	+	+	+
- <sup>†</sup> Oligo- or anovulation and hyperandrogenemia (B)	+	+	-
- <sup>v</sup> Ovulatory PCOS (C)	-	+	+
- <sup>£</sup> Mild PCO (D)	+	-	+

## Genetic?/ familial?

 PCOS might be a complex multigenic disorder with strong epigenetic and environmental influences as diet and other lifestyle issues.

(Nature Review endocrinology 2018)

 PCOS hyperandrogenic symptoms and ultrasound picture are more frequent in 1<sup>st</sup> degree relatives compared with controls and serum AMH in prepubertal daughters of women with PCOS increases.

AMH: antimullerian hormone 2006)

(Sir-Petermann et al.,

## Complex syndrome



## Clinical picture

#### Reproductive manifestations:



- Hyperandrogenism (Acne, Male pattern baldness, Hirsutism
  - etc...), menstrual dysfunction and anovulation.

#### > Obstetric manifestations:

Early pregnancy loss, gestational diabetes, induced hypertension.



(Teede h et al., 2010).

#### (Goodman et al., 2015)

## Clinical picture (cont.)

Metabolic manifestations: obesity, insulin resistance, Impaired Glucose Tolerance, DM, and metabolic syndrome.

(Cobin et al., 2015)





# Biochemical Manifestations of PCOS



ASD: androstenedione SHBG: sex-hormone binding globulin GTT: glucose tolerance test LH: leutinizing hormone FSH: follicle stimulating hormone DHEAS: Dehydroepiandrostenedione sulfate Part of contemporary endocrinology series by Adam Balen





# Impact of obesity on PCO

- Obesity excessive weight that may impair health is seen in approximately 60% of cases and amplifies the severity of PCOS presentation. (Legro et al., 2004)
- It can be measured by BMI (kg/m<sup>2</sup>) published by both the (WHO) and (NICE) and accordingly;

<18.5: Underweight 18.5-24.9: Normal/Healthy

25.0-29.9 : Overweight (pre-obese) 30.0-34.9 : Obese (Class I)

35.0-39.9 : Obese (Class II) ≥40 Obese (Class III = morbid obesity)

**BMI**: Body Mass Index

WHO: World Health Organization

NICE: National Institute for health and Care Excellence

- Waist hip ratio is another important measure which correlates more with the metabolic disorder
  - (Fleir et al., 2004)

- The prevalence of obesity varies according to geographic location: it is greater in the USA than in other places.
  - (Carmina et al., 2003)

Adipose tissue is a well-known source of inflammation and is considered as a complex and highly active endocrine organ which produces various adipokines and cytokines which are involved in the regulation of many processes such as inflammation, type 2 diabetes mellitus (T2DM) and other cardio metabolic diseases.

(Gulcelik et al., 2009)

 PCOS is a chronic low-grade inflammation contributing to the main pathogenesis of its long-term consequences.

(Repaci A et al., 2011)

 Inflammatory mediators in PCOS were linked to hyperandrogenism, insulin resistance, T2DM, obesity, and cardiovascular risk factors.

(Duleba AJ et al., 2012)

The <u>prevalence of PCOS</u> appears to be <u>rising</u> among adolescent and young women due to the <u>current epidemic</u> <u>of obesity, worldwide</u>.

•

 Compared with normal weight women with PCOS, <u>obese</u> <u>women with PCOS</u> have worsened <u>hyperandrogenic and</u> <u>metabolic state</u>, <u>Poorer menses</u>, <u>ovulation & pregnancy</u> rate.

(Hojlund 2014)

- The distribution of body fat is more important than the actual body weight.
- Visceral fat is more metabolically active, and an increased waist: hip ratio correlates better with both metabolic risk and long term disease.
  - (Hojlund 2014)

- In women with PCOS and a BMI >35kg/m2, 20% of pregnancies end with stillbirth and another 20% has congenital anomalies.
- The <u>supposed mechanism</u> for these increased rates includes <u>insulin resistance</u> and <u>impending or undiagnosed</u> <u>diabetes</u>.
  - (Hojlund 2014)

- Weight loss & exercise in women with PCOS improves the endocrine profile, cycle regularity, ovulation rate & the likelihood of a healthy pregnancy.
- Even a loss of 5% 10% of total body weight can achieve
   30% reduction of central fat, an improvement in insulin sensitivity and restore ovulation.
  - (Hojlund 2014)

#### **Can Obesity Cause PCOS?**

eproductive disturbances are more common in obese omen regardless of the diagnosis of PCOS. Furthermore, COS has abnormalities in the gonadotropin hormone leasing hormone, leading to preferential increase in LH lease over FSH. These abnormalities are independent of pesity.

(sam et al., 2003)

(Alvarez-Blasco et al., 2006)

#### **Does PCOS Cause Obesity?**

 By using dual-energy X-ray absorptiometry, there was increased accumulation of central fat in women with PCOS.

(Macruz et al., 2017)

 Chronic exposure to higher testosterone levels in women with PCOS may modify body fat distribution in these women.

(Diri et al., 2017)

few studies have examined visceral fat content in women with PCOS. Studies of isolated abdominal fat cells from women with PCOS have revealed larger-sized cells in both obese and nonobese women with PCOS compared to control women, suggesting a preferential abdominal accumulation of adipose tissue.

> (Dunaif et al., 1992) (Diri et al., 2017)

## Long Term Risks Associated with PCOS

### **Metabolic Syndrome**

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Hypertension	Current antihypertensive therapy and/or BP>130/85mmHg	metabolic syndrome in women with PCOS is
Dyslipidemia	Plasma Triglyceride level >150mg/dl and/or HDL level <50 mg/dl	approximately 43-46%.
Obesity	Waist Circumference >88cm	(Kim et al., 2014)
Glucose	Fasting Blood Glucose level >110mg/dl	
Requirements for Diagnosis	Any 3 of the above disorders	

## **Insulin Resistance**

 Insulin resistance is found in PCOS, with prevalence being estimated in 50-70% of cases and is independent of obesity.

(Vigil et al., 2007)

(Rumina et al., 2013)

## Impaired Glucose Tolerance and Diabetes Mellitus

 Of obese women with PCOS, 10% have undiagnosed diabetes and 35% have impaired glucose tolerance.

(Parker and Semple 2013)



**Source of Image:** Teede, Helena j. et al., Assessment and management of polycystic ovary syndrome: summary of an evidence-based guideline, *Med J Aust* 2011; 195 (6): S69.

## Lifestyle Modification and Weight Loss in PCOS

 All strategies for weight loss, including surgery, the combination of weight-reducing medications and group lifestyle modification was shown to be more effective than either alone, in a group of obese adults.

(Legro et al., 2016)

## Lifestyle Modification and Weight Loss in PCOS

- Bariatric surgery is of great benefit in PCOS patients to reverse much of the metabolic & reproductive problems in them, including hirsutism.
- Testosterone and DHEAS decreased; amelioration of IR occurred and ovulatory cycles were also restored.
  - (Lagana et al., 2018)

**DHEAS:** Dehydroepiandrostenedione Sulfate

**IR**: Insulin Resistance

## **Conclusion**

- PCOS is a commonly encountered endocrinopathy in women of reproductive age.
- Obesity is a common finding in PCOS and aggravates many of its reproductive and metabolic features.
- The relationship between PCOS and obesity is complex, not well understood, and most likely involves interaction of genetic and environmental factors.

