



Biomarkers of ovarian cancer & cysts

Reproductive Block



Objectives



Discuss the risk factors and possible causes of polycystic ovarian syndrome (PCOS) and ovarian cancer



Comprehend the role of insulin resistance and hypersecretion of androgens in the development of PCOS



Identify avenues for the diagnosis and treatment of PCOS and ovarian cancer



Assess the diagnostic significance of CA-125 in ovarian cancer

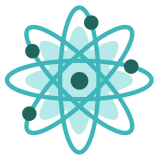


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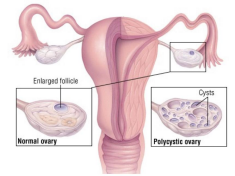


Polycystic Ovarian Syndrome (PCOS)

Polycystic Ovarian Syndrome (PCOS)

- Formation of multiple small cysts in the ovaries. In ultrasound: # of cysts ≥ 12 or more.
- Affects 5-10% of women (20% in some populations).
- A major cause of infertility in women.

Usually size of the ovaries increases + presence of multiple immature cysts (immature follicles) which started growing but could not become mature. Their growth became arrested due to impaired levels of hormones



Polycystic Ovarian Syndrome

Strongly correlated to

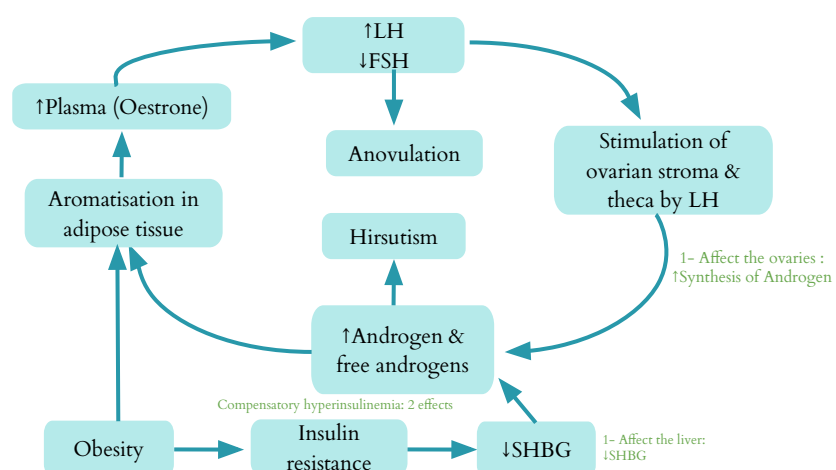
- Family history.
- Obesity (40%).
- Hirsutism.
- Chronic anovulation.
- Glucose intolerance.
- Hypersecretion of luteinizing hormone (LH) and androgens (testosterone). Usually we do not measure LH alone. Ratio of LH to FSH is imp. Normally, FSH is higher. In PCOS, LH is 2 times FSH (2:1)
- Low levels of SHBG (sex hormone-binding globulin). Normally, 80% of androgens are bound to SHBG. 18-19% bound to albumin, and 1-2% are free. In PCOS, \downarrow SHBG \rightarrow \uparrow free androgens (testosterone) \rightarrow show effect
- Insulin resistance.
- Hyperlipidemia. (obesity related)
- Hypertension.
- Menstrual disorders.

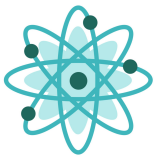
Causes

Probable causes:

- Exact cause of the syndrome is unknown.
- May be multifactorial (genetic and environmental).
- **Insulin resistance** causes excessive androgen production in ovaries (common).
- **Abnormalities** in ovaries, adrenal and pituitary glands.

Endocrine changes in PCOS





Polycystic Ovarian Syndrome (PCOS)

Polycystic Ovarian Syndrome (PCOS)

Diagnosis

- **Diagnostic criteria for PCOS :**

European Society for Human Reproduction & Embryology (ESHRE) and American Society for Reproductive Medicine (ASRM) recommendation:

- **At least two of the following features are required for PCOS diagnosis:** (for adults; in case of teenagers, all 3 features should be present to diagnose PCOS.)

1. **Oligo-ovulation or anovulation** manifested as oligomenorrhea or amenorrhea.
2. **Hyperandrogenism** (clinical and biochemical evidence of androgen excess).
3. **Polycystic ovaries** (as defined by ultrasonography).

- **Diagnosis done by measuring :**

1. **Free testosterone:**

Total testosterone is less sensitive, increased androgens in PCOS.

2. **Sex hormone-binding globulin:**
(SHBG; decreased in PCOS)

3. **Luteinizing hormone:**

(LH; high in 60% cases) LH to FSH ratio is more important

4. **Follicle stimulating hormone:**

Normal or low

5. **Fasting blood glucose**

6. **Insulin**

7. **Lipids**

- **Ovarian ultrasound :**

30% of patients do not have ovarian cysts despite having symptoms

Treatment

Aim of treatment: interrupt the cycle of obesity, insulin resistance, excess androgens

- Reduce LH levels (by oral and contraceptives)

Combination of estrogen & progesterone

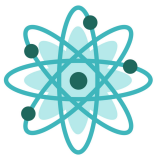
- **Reduce body weight**

- Increase FSH levels (by clomiphene, etc.)

Latest drug is letrozole, an aromatase inhibitor

- Estrogen replacement therapy:

- In select women after careful risk counseling (Risk of developing cancer)



Ovarian Cancer

- A leading cause of death because of gynecologic cancer
- Due to **malignant** transformation of ovarian epithelial cells
- Most common type of ovarian cancer

Ovarian Cancer Subtypes:

1

Serous (46%):
surface epithelial
tumors

2

Mucinous (36%)
Mucinous epithelial
tumors

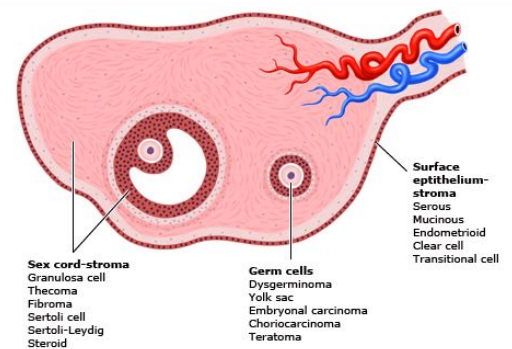
3

Endometrioid (8%):
endometrial
tumors

Ovarian Cancer Risk factors:

- Nulliparity (woman with no childbirth or pregnancy)
Increase in Age is a risk factor and its important.
- Family history of breast, ovarian, colorectal cancer
(first degree relatives).
- Mutations in **BRCA1** and **BRCA2** genes (most common).
- Carriers of **BRCA1** mutations have a risk 44% .
- Premenopausal breast cancer or ovarian cancer indicates higher risk for hereditary.
- **Ashkenazi Jews** have higher risk of ovarian cancer.

Origins of ovarian tumors



Some epithelial ovarian carcinomas may originate in the fallopian tube epithelium.

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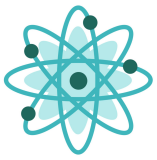
Biomarkers & Diagnosis:

Epithelial ovarian cancer is commonly diagnosed at a later stage, Due to non-specific symptoms such as abdominal pain, bloating, early satiety, nausea, etc.

Most patients (75%) have advanced-stage tumor upon diagnosis

◆ Diagnosis includes:

- History taking *Age of menarche, Pregnancy, Family history*
- Physical examination *pelvic mass*
- Ultrasound *cysts maybe not detected cuz very small*
- Measurement of serum CA-125 levels *should be significantly high along with the previous factors*



Cancer Antigen 125 (CA-125)

1

The only serum marker of epithelial ovarian cancer

2

A cell surface glycoprotein expressed in the epithelium of all tissues.
Normally absent in serum

3

CA-125 is elevated in ovarian cancer **>35 U/ml is considered positive**

4

Recommended as an annual test for women with family history of ovarian cancer

5

CA-125 is associated with stages of ovarian cancer

- **A non-specific marker**
- **False positive CA-125 conc. are found in benign conditions such as:**
 1. Endometriosis
 2. Uterine leiomyomas
 3. Pelvic inflammatory disease
 4. During the first trimester of pregnancy
 5. During menstruation
- Some patients (< 50 years) have elevated CA-125 due to unrelated malignant mass.
- **CA-125 is not a marker of choice for ovarian cancer screening due to:**
 - ❖ Low prevalence of ovarian cancer
 - ❖ High false-positive rate

CA-125 Elevated in:

50%

90%

>90%

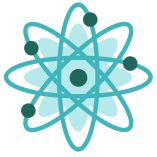
⊙ 50% of patients with stage I ⊙ 90% of patients with stage II ⊙ >90% of patients with stage III and IV

CA-125 Useful in:

Monitoring patient's
response to chemotherapy

Success of surgery
(de-bulking procedures)

Annual testing for
women with family
history of ovarian cancer



Take Home Message



PCOS is strongly correlated to insulin resistance and endocrine abnormalities.



Although a nonspecific biomarker, CA-125 is important for staging and follow-up of ovarian cancer treatment

MCQs

Q1. In which of the following can the levels of CA-125 be useful?

A. Monitoring patient response to chemotherapy.	B. Biomarker for PCOS.	C. Associated with high risk of ovarian cancer.	D. Marker of choice for ovarian cancer.
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Q2. PCOS is treated by ?

A. Progesterone replacement therapy.	B. Estrogen replacement therapy	C. Decrease FSH levels	D. Increase LH levels
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Q3. How to treat PCOS?

A. Reduce FSH	B. Reduce LH	C. Decrease estrogen	D. Decrease insulin sensitivity
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Q4. False positive CA-125 concentration are found in all of the following conditions EXCEPT?

A. Endometriosis	B. uterine leiomyoma	C. pelvic inflammatory disease	D. ovarian cancer
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Q5. Which ONE of the following is the cause of ovaries to produce androgens in case of PCOS?

A. High levels of FSH	B. Coeliac disease	C. Insulin resistance	D. Ovarian cyst
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Q6. Which of the following stages of ovarian cancer in which 50% of people have high CA-125?

A. Stage 1	B. Stage 2	C. Stage 3	D. Stage 4
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A1. A A2. B A3. B A4. D A5. C A6. A

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