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Review on Ovarian Cancer

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Abstract:
Ovarian cancer is a deadly gynecologic cancer, often diagnosed late due to vague symptoms, leading to poor survival, but improved treatments like surgery, platinum chemo, and targeted drugs (PARP inhibitors, bevacizumab) are increasing survival, especially with genetic awareness (BRCA mutations). Most cases (90%) are epithelial, primarily high-grade serous, with key risk factors being age, genetics (BRCA1/2), family history, and nulliparity, while oral contraceptives and childbirth reduce risk. Treatment involves cytoreductive surgery and chemotherapy, with maintenance targeted therapies and new approaches for recurrence

Keywords: **Ovarian Cancer, Female Reproductive System, Fallopian Tubes, Estrogen, Progesterone**

INTRODUCTION

Ovarian cancer is one of the most serious malignancies affecting the female reproductive system. It begins in the ovaries—small, almond-shaped organs responsible for producing eggs and the hormones estrogen and progesterone. Because early-stage ovarian cancer often develops without noticeable *symptoms*, most cases are diagnosed only after the disease has advanced. This late detection makes ovarian cancer one of the leading causes of cancer-related deaths among women worldwide.The disease can arise from different types of ovarian cells, leading to several subtypes, among which epithelial ovarian cancer is the most common. Risk factors include age, family history, genetic mutations such as BRCA1 or BRCA2, infertility, hormonal factors, and lifestyle influences. Despite significant improvements in surgical techniques and chemotherapy, early detection remains the biggest challenge, and ongoing research focuses on developing better screening tools, targeted therapies, and personalized treatment approaches.Because symptoms—such as abdominal bloating, pelvic pain, and changes in appetite—are often vague or easily mistaken for other conditions, awareness and timely medical evaluation play a crucial role in improving survival outcomes.

ANATOMY OF THE FEMALE REPRODUCTIVE SYSTEM

The female reproductive system is designed for oogenesis (formation of ova), fertilization, pregnancy, childbirth, and hormone production**.** It is divided into internal reproductive organs and external genitalia**.**

1. Ovaries

The ovaries are a pair of almond-shaped organs located on either side of the uterus.

Structure

- **Cortex** – contains ovarian follicles at different stages of development.
- **Medulla** – contains blood vessels, nerves, and connective tissue.

Functions

- Produce ova (eggs)**.**

Secrete hormones:

- Estrogen
- Progesterone

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These hormones regulate puberty, menstruation, pregnancy, and secondary sexual characteristic.

2. Fallopian Tubes (Uterine Tubes)

Tubular structures that connect the ovaries to the uterus.

Parts

1. **Fimbriae** – finger-like projections that collect the ovum.
2. **Infundibulum** – funnel-shaped section.
3. **Ampulla** – widest part; site of fertilization**.**
4. **Isthmus** – narrow region leading to uterus.

Function

- Transport of ova from ovary to uterus.
- Site of sperm–egg fusion (fertilization)**.**

3. Uterus:

A hollow, muscular, pear-shaped organ located in the pelvic cavity.

Parts:

- **Fundus** – upper rounded area.
- **Body** – main central region.
- **Cervix** – lower narrow portion opening into vagina.

Uterine Wall Layers

1. **Endometrium** – inner lining; thickens during menstrual cycle; sheds during menstruation.
2. **Myometrium** – thick muscular layer responsible for labor contractions.
3. **Perimetrium** – outer serous layer.

Functions

- Implantation of fertilized egg.
- Nourishment of fetus.
- Labor and childbirth.

4. Cervix

The lower cylindrical portion of the uterus.

Features

- **Internal os** – opening from uterus.
- **External os** – opening to vagina.
- Produces cervical mucus, which changes consistency during menstrual cycle.

Functions:

- Passageway between uterus and vagina.
- Protects uterus from infection.
- Dilates during childbirth.

5. Vagina

A muscular, elastic canal from cervix to the external environment.

Functions:

- Birth canal.
- Receives the penis during intercourse.
- Passage for menstrual flow.

6. External Genitalia (Vulva)

Consists of:
(a) Mons Pubis:Fatty pad covering pubic bone
(b) Labia Majora:Outer folds protecting internal structures.
(c) Labia Minora:Inner folds surrounding vestibule.
(d) Clitoris:Highly sensitive erectile tissue; homologous to male penis.
(e) Vestibule:Contains openings of urethra and vagina.
(f) Bartholin's Glands:Produce lubricating fluid.

7. Mammary Glands (Breasts)

Though not part of the internal reproductive tract, they are secondary reproductive organs.

Function:

- Produce milk for breastfeeding.

Diagram:

You can include:

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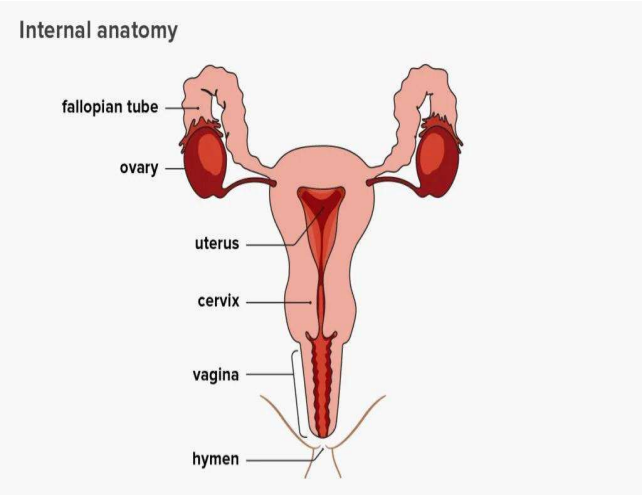
- Ovaries
- Fallopian tubes
- Uterus
- Cervix
- Vagina
- Vulva structures



TYPES OF OVARIAN CANCER

Ovarian cancer is not a single disease. It includes several distinct tumor types, each arising from different cells within the ovary. The World Health Organization (WHO) classifies ovarian cancers into three major groups:

1. Epithelial Ovarian Tumors

These arise from the surface (epithelial) coating of the ovaries.
They are the most common type, responsible for 85–90% of ovarian cancers.

a) Serous carcinoma

- Most common subtype (high-grade serous carcinoma is the most aggressive)
- Often diagnosed at a later stage
- Thought to originate from the fallopian tube epithelium

b) Mucinous carcinoma

- Contains mucus-producing tumor cells
- Less common
- Can resemble gastrointestinal tumors

c) Endometrioid carcinoma

- Associated with endometriosis
- Usually detected at an earlier stage

d) Clear cell carcinoma

- Also linked to endometriosis
- More resistant to chemotherapy

e) Transitional (Brenner) tumor

- Rare
- May resemble bladder (urothelial) cells

2. Germ Cell Tumors

These originate from the egg-producing cells of the ovary.
More common in children and young women.
Common types:

- **Dysgerminoma** – most common germ cell cancer
- Yolk sac tumor (endodermal sinus tumor)
- Immature teratoma
- Embryonal carcinoma
- Choriocarcinoma (non-gestational)

These tumors often grow quickly but respond very well to chemotherapy.

3. Sex-Cord Stromal Tumors

These arise from the connective tissues that hold the ovary together and produce hormones.
Major subtypes:

- Granulosa cell tumor (produces estrogen; can cause menstrual changes)
- Thecoma
- Fibroma
- Sertoli-Leydig cell tumor (produces male hormones)

These cancers are usually slow-growing and diagnosed earlier.

CAUSES AND RISK FACTORS OF OVARIAN CANCER

Ovarian cancer develops when abnormal cells in the ovaries begin to grow uncontrollably. Although the exact cause is not fully understood, doctors have identified several risk factors that increase the likelihood of developing this cancer.

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1. Causes of Ovarian Cancer

The exact biological cause is unknown, but ovarian cancer is believed to develop due to a combination of genetic, hormonal, and environmental factors.

a) Genetic Mutations

Some ovarian cancers are caused by inherited mutations:

- **BRCA1 and BRCA2 gene mutations**
- **Lynch syndrome (HNPCC)**

These mutations increase the chance of abnormal cell growth in the ovaries.

b) Age-related DNA Damage

As women age, their cells accumulate DNA changes. These mutations can eventually lead to cancer.

c) Hormonal Influence

Long-term exposure to estrogen (without progesterone) may stimulate cell growth in the ovaries.

2. Risk Factors of Ovarian Cancer

1. Age

- Most common in women above 50 years, especially after menopause.

2. Family History

- Having a mother, sister, or daughter with ovarian or breast cancer increases the risk.

3. Inherited Genetic Mutations

- BRCA1 and BRCA2
- Genes linked to Lynch syndrome
- RAD51C, RAD51D, BRIP1 (less common)

4. Reproductive History

- Higher risk for women who:
  - Never had children
  - Had their first pregnancy after age 35
  - Had early menstruation (before 12)
  - Had late menopause (after 52)

More ovulation cycles = slightly higher risk.

5. Hormone Replacement Therapy (HRT)

- Long-term use of estrogen-only therapy after menopause may increase risk.

6. Endometriosis

A condition where the tissue lining the uterus grows outside it. This increases the risk of clear cell and endometrioid ovarian cancers.

7. Obesity

- Overweight women (BMI ≥ 30) have a higher risk and poorer outcomes.

8. Use of Fertility Drugs

- Some studies show a slight risk increase for women who used ovulation-stimulating drugs for many years.

9. Smoking

- Increases risk of mucinous ovarian cancer in particular.

10. Environmental/Lifestyle Factors

- Long-term exposure to talcum powder in the genital area (debated but mentioned in some studies)
- Diet low in vegetables and fiber (minor link)

Protective Factors (Reduce Risk)

These factors lower the risk of ovarian cancer:

1.Pregnancy and breastfeeding

Fewer ovulation cycles = lower risk.

2.Oral contraceptive pills

Using birth control pills for 5+ years can reduce risk by up to 50%**.**

3.Tubal ligation or hysterectomy

These surgeries reduce risk.

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4. Maintaining a healthy weight

SIGNS AND SYMPTOMS

Ovarian cancer signs often mimic other conditions, including persistent bloating, pelvic/abdominal pain, feeling full quickly, frequent urination, fatigue, and changes in bowel habits (constipation/diarrhea). These symptoms are usually non-specific and become more noticeable as the cancer progresses, emphasizing the need for medical evaluation if persistent, as early detection significantly improves outcomes.

Common Symptoms

- **Abdominal Issues:** Bloating, swelling, pressure, or pain in the abdomen or pelvis.
- **Digestive Changes:** Feeling full quickly, loss of appetite, indigestion, gas, constipation, or diarrhea.
- **Urinary Changes:** A sudden or frequent urge to urinate.
- **Fatigue:** Unusual tiredness or low energy levels.
- **Pain:** Pelvic or lower back pain.
- **Menstrual/Vaginal Changes:** Abnormal bleeding or discharge (more common with rare tumor types).

When to See a Doctor

- Symptoms that are new, persistent, and occur frequently (e.g., more than 12 times a month).
- Symptoms that don't go away or worsen.

Important Considerations

- **Non-Specific:** These symptoms can be caused by many other less serious conditions, like indigestion or a stomach virus, which can delay diagnosis.
- **Early Stage:** Early-stage ovarian cancer is often asymptomatic, with symptoms appearing as the disease advances.
- **Diagnosis:** A doctor may use physical exams, imaging (ultrasound, CT), and blood tests (like CA-125) but often needs a biopsy (tissue sample) for a definitive diagnosis.

STAGES OF OVARIAN CANCER (FIGO STAGING SYSTEM)

Ovarian cancer staging is based on the FIGO (International Federation of Gynecology andObstetrics) and TNM systems. Staging helps doctors understand how far the cancer has spread and guides treatment decisions.

Stage I – Cancer limited to the ovaries or fallopian tubes

Stage IA:Cancer is in one ovary or one fallopian tube only.Tumor is inside the ovary/tube; the outer capsule is intact.
Stage IB:Cancer is in both ovaries or both fallopian tubes, but limited to them.

Stage IC:Cancer is in one or both ovaries/tubes with additional findings:
IC1: Surgical spill of cancer cells during surgery
IC2: Capsule is ruptured before surgery OR cancer on the ovary/tube surface
IC3: Cancer cells found in peritoneal fluid (abdomen fluid)
Stage II – Cancer has spread to nearby pelvic organs
Stage IIA-Cancer has spread to the uterus or fallopian tubes or other pelvic organs.
Stage IIB-Cancer involves other pelvic tissues, such as bladder, rectum, or pelvic peritoneum.
Stage III – Cancer has spread to the abdomen or lymph nodes
Stage IIIA1-Cancer has spread to pelvic or para-aortic lymph nodes only.
Stage IIIA2:Microscopic cancer deposits found outside the pelvis (upper abdomen), not visible to the naked eye
Stage IIIB-Visible cancer deposits in the abdomen ≤ 2 cm in size.
Stage IIIC-Visible cancer deposits in the abdomen > 2 cm orCancer has spread to the liver or spleen surfaces (but not inside the organs).
Stage IV – Distant metastasis (cancer has spread outside the abdomen)
Stage IVA-Cancer cells present in fluid around the lungs (pleural effusion).
Stage IVB-Distant organ spread such as:

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Liver (inside the liver tissue)
Lungs
Bones or brain
Distant lymph nodes (inguinal, supraclavicular etc.)

DIAGNOSIS AND TESTS FOR OVARIAN CANCER

Diagnosing ovarian cancer can be challenging because early-stage disease rarely causes obvious symptoms. Therefore, doctors rely on a combination of clinical evaluation, imaging tests, blood markers, and sometimes surgical procedures to confirm the diagnosis.

Pelvic Examination

1.A pelvic exam helps the doctor feel:

The uterus
The ovaries
The fallopian tubes
Surrounding tissues

2. Imaging Tests

Imaging helps visualize the ovaries and surrounding structures.

a) Transvaginal Ultrasound (TVUS)

Primary imaging tool
Gives detailed images of ovaries
Identifies cysts, solid masses, or abnormal shapes
Helps distinguish benign vs suspicious tumors

b) Abdominal/Pelvic Ultrasound

Used when TVUS is not enough or when evaluating larger areas.

c) CT Scan (Computed Tomography)

Detects spread (metastasis) to lymph nodes, abdomen, liver, or lungs
Helpful for surgical planning

d) MRI (Magnetic Resonance Imaging)

Provides highly detailed soft-tissue images
Used when ultrasound findings are unclear

4.Biopsy

For suspected ovarian cancer, biopsy is usually NOT done before surgery, because:
It can spread cancer cells
Most diagnoses are made during surgery
However, biopsy is done when:
Surgery is not possible
Cancer has already spread widely
Diagnosis is needed before chemotherapy

Treatment options

Ovarian cancer treatment primarily combines aggressive surgery (cytoreduction) to remove visible tumors with platinum-based chemotherapy (carboplatin/paclitaxel), often followed by maintenance therapy like PARP inhibitors or anti-angiogenics (bevacizumab) for advanced stages, with newer options including targeted agents (FRα-ADCs) and immunotherapies. The Indian Council of Medical Research (ICMR) offers detailed guidelines in a downloadable PDF, while resources from the CDC, NIH, and American Cancer Society provide comprehensive overviews, with many clinical trials and reviews available on {Link: PubMed and {Link: MDPI for deeper dives.

Core Treatments

- **Surgery:** The cornerstone involves cytoreductive surgery to remove as much cancer as possible, sometimes including neoadjuvant chemotherapy (before surgery) for poor surgical candidates, followed by interval debulking surgery.
- **Chemotherapy:** Usually includes platinum drugs (carboplatin) and taxanes (paclitaxel).
- **Maintenance_Therapy:** Drugs like PARP inhibitors (for BRCA-mutated cancers) or anti-angiogenic drugs (like bevacizumab) are used after initial chemo to prevent recurrence.

Newer & Targeted Options PARP_Inhibitors: (e.g., Olaparib, Niraparib) Exploit DNA repair defects, especially in BRCA-mutated cancers.

- **Anti-Angiogenics:** (e.g., Bevacizumab) Target blood vessel formation.
- **Targeted Antibodies:** Mirvetuximab soravtansine (FRα-ADC) for tumors with high folate receptor alpha expression.

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- **Hormonal Therapy:** May benefit some low-grade serous cancers.
- While there is no single way to entirely prevent most ovarian cancers, certain lifestyle modifications and medical interventions can significantly lower the risk. The general approach focuses on reducing modifiable risk factors and managing overall health.

Prevention and Lifestyle Modifications

- Maintaining a healthy weight through diet and regular exercise is important. Aim for at least 150 minutes of moderate aerobic activity or 75 minutes of vigorous activity each week. A healthy diet rich in fruits, vegetables, whole grains, and lean proteins is recommended, while limiting processed foods, red meats, and sugary beverages may be beneficial. Quitting smoking, especially important for the mucinous subtype, can significantly reduce risk. Resources for quitting are available through public health organizations like the CDC. Limiting long-term use of hormone replacement therapy (HRT) after menopause may also lower risk.

Medical and Reproductive Factors

- Long-term use of oral contraceptives has been shown to significantly reduce the risk of ovarian cancer, with the protective effect lasting for years. Having a full-term pregnancy or breastfeeding can also lower risk. Genetic counseling and testing for mutations like *BRCA1* and *BRCA2* are available for those with a strong family history. For women at very high risk due to genetic mutations, preventive surgery such as a bilateral salpingo-oophorectomy (removal of ovaries and fallopian tubes) can reduce risk by up to 95%. Tubal ligation or a hysterectomy may also lower risk. While there is no standard screening test for the general population, regular gynecological exams and being aware of persistent symptoms are important for earlier detection.

COMPLICATIONS

- Ovarian cancer and its treatments can lead to various complications, broadly categorized into issues caused by the advanced cancer itself (such as fluid accumulation and bowel obstruction) and side effects resulting from treatment (like infection, nerve damage, or early menopause).

1.Complications Caused by Ovarian Cancer

- **Fatigue and weakness** (a very common symptom in advanced stages).
- **Nutrition issues** due to nausea, vomiting, loss of appetite, and feeling full quickly.
- **Pain** in the pelvic and/or abdominal areas.
- **Weight loss or gain**.

2.Complications from Treatment

- **Infection** at the surgical site or in the chest/lungs.
- **Bleeding** internally or externally.
- **Blood clots** (deep vein thrombosis or pulmonary embolism).
- **Damage to nearby organs** like the bladder, bowel, or ureters.
- **Lymphedema** (swelling in the legs) if lymph nodes are removed.
- **Hernias** at the incision site.

3.Chemotherapy Complications

- Chemotherapy drugs affect rapidly dividing cells, including healthy ones, leading to side effects:
- Bone marrow suppression, leading to anemia (fatigue), leukopenia (increased infection risk), and thrombocytopenia (easy bruising/bleeding).
- Nausea, vomiting, and diarrhea or constipation.
- Peripheral neuropathy (nerve damage causing numbness, tingling, or pain in hands/feet).

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- Hearing loss or kidney damage (especially with cisplatin).
- Hair loss**.**
- **"Chemo brain"** (cognitive issues like memory or concentration problems)

CONCLUSION:

OC is a leading cause of cancer incidence and mortality worldwide. This review describes the magnitude of the problem and summarizes epidemiological studies that have identified genetic, environmental, and lifestyle factors that may increase and decrease risk of this lethal disease. These factors have likely impacted the diverse patterns and trends of OC incidence and mortality seen across the globe. Increased and earlier use of oral contraceptives has very likely contributed to the declining trends observed in most developed countries while reduced parity and changes in diet and physical activity could play a role in the increasing trends observed in several countries with economic growth.

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