INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Review Article

A Review Article On: Ovarian Cancer

Rutuja Shingare*, Bhanage Pratik, Dr. Megha Salve

Shivajirao pawar college of pharmacy pachegaon

ARTICLE INFO

Published: 24 Nov. 2024
Keywords:
ovarian carcinoma; epidemiology; diagnosis; prognosis; treatment.
DOI:
10.5281/zenodo.14210652

ABSTRACT

Ovarian cancer remains a deadly and lethal form of gynecological cancer that impacts both younger and older women. Understanding different elements that could cause ovarian cancer and how they contribute to its advancement, spread and endurance could assist in its care and avoidance. This paper intends to examine various genetic and environmental risk factors associated with the onset of ovarian cancer and how they function. The study's research methods adhere to the principles specified by. It is a thorough assessment of risk factors for ovarian cancer in the literature. The theoretical foundation of the paper was established by examining the involvement of genetics and environmental risk factors in ovarian carcinogenesis and their mechanisms. A new framework is introduced to encompass the highly dynamic interplay between ovarian carcinogenesis and the actions of certain related risk factors. The aim of the study is to examine and condense the theoretical and empirical information to stimulate fresh conversations and guide future research efforts. The model focuses on different factors that can initiate the occurrence of ovarian cancer such as TP53, BRCA genes, smoking, and talcum powder, and how they contribute to the progression of ovarian cancer. Numerous studies have investigated how changes in specific genes and environmental influences can contribute to the development of ovarian cancer. More studies are required to gain a deeper understanding of how their method of operation works. The information presented in this document can aid in improving screening, treatment, and prevention for ovarian cancer. This research presents a promising chance to enhance our understanding of ovarian cancer, helping medical professionals and researchers develop improved strategies for preventing and treating the disease.

INTRODUCTION

Ovarian cancer is a diverse group of tumors that is the seventh deadliest cancer in women globally and the eighteenth most common overall, being a leading cause of gynecological cancer deaths in the western world. It has been previously proposed that the majority of ovarian carcinomas originate from the ovarian surface epithelium or inclusion

***Corresponding Author:** Rutuja Shingare
Address: *Shivajirao pawar college of pharmacy pachegaon.*
Email ✉: rutujashingare580@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

cysts formed after follicular rupture and repair[1]. Each year, around the globe, 204,000 women are found to have ovarian cancer and 125,000 women lose their lives to this illness[2]. Epithelial ovarian carcinomas (EOC) account for approximately 90-96% of all cases. Seventy-five percent of patients are diagnosed with advanced disease because of inadequate screening methods and limited early symptoms[3]. Clinical remission can be reached for as many as 80% of women through debulking surgery combined with chemotherapy. However, relapse typically occurs, causing the disease to worsen and ultimately resulting in death[4]. The typical age for developing ovarian cancer is 63 years old, which falls within the 6th and 7th decade of life, and the likelihood of occurrence rises as age advances[3]. Different studies and group studies on the correlation between TP53 and ovarian cancer have also demonstrated that mutations in the tumor suppressor 53 gene can raise the likelihood of developing ovarian cancer. TP53 is a gene that suppresses tumors, controlling cell growth to prevent it from becoming uncontrolled; mutations in TP53 can cause ovarian development [5]. The most common barrier to achieving a favorable life expectancy in most countries is currently present. Ovarian cancer is the third most common gynecologic cancer following cervical and uterine cancer. The data indicates that eliminating and reducing risk factors can prevent 33% to 40% of all cancer cases[6]. At present, there are no clear protocols for treating ovarian cancer in mothers. On the other hand, the correct management includes performing staging laparotomy, debulking surgery, and adjuvant chemotherapy, or obtaining a tissue diagnosis with initial chemotherapy, then proceeding with later debulking surgery. Chemotherapy is not recommended during the first trimester of pregnancy, but may be given during the 2nd and 3rd trimesters on a case-by-case basis, although it is still considered controversial. Management varies depending on the case and requires a team approach involving multiple disciplines. It depends on the length of pregnancy, the severity of the illness, plans for future fertility, and the mother's decision to proceed with the pregnancy [7].

Risk Factor:

Various influences play a role in the occurrence of ovarian cancer; among them, a history of breast and ovarian cancer in the family is a significant risk factor supported by epidemiological research. The likelihood of contracting the disease may also relate to age and other aspects of the environment. However, current evidence does not definitively link ovarian carcinoma to exposure to carcinogens in industrial settings or therapeutic radiation[8].

The strongest risk factor is

- A women with a single first-degree relative with ovarian cancer has a relative risk (RR) of approximately 3.6 for developing ovarian cancer compared with general population.
- Her life time risk approximately 5%.
- 5-10% of ovarian cancer are linked to identifiable, inherited mutations in certain genes.
- Families in which three or more first-degree relatives have ovarian or ovarian plus breast cancer are likley to have a cancer-susceptibility genetic mutation that is transmitted in an autosomal-dominant inheritance pattern[9].

There are numerous reproductive and genetic risk factors for the development of ovarian cancer. The likelihood of getting ovarian cancer rises in women who have never given birth, are older than 35 when they have their first child, have a history of pelvic inflammatory disease, and are using hormone replacement therapy[10]. These results provide evidence for the "incessant ovulation" theory. According to this theory, continuous ovulation can increase the risk of ovarian cancer by harming the ovaries' epithelium; thus, any

factor that decreases ovulation can help prevent ovarian cancer[11]. Findings from a research in Canada showed that using hormonal contraceptive pills is linked to a notable decrease in all types of epithelial ovarian cancer, with the exception of mucinous tumors. As indicated by the results of this research, the odds ratio for one year of pill usage was 0.89 [0.85–0.93] for non-mucinous tumors and 0.98 [0.93–1.04] for mucinous tumors[12]. Women with a family history of two or more first-degree relatives with ovarian cancer, along with BRCA1 and BRCA2 gene mutations (Hereditary Breast Ovarian Cancer [HBOC] syndrome), or families impacted by Lynch syndrome Hereditary nonpolyposis colorectal cancer (HNPCC), typically experience early onset ovarian cancer[13]. Having a family history of ovarian, breast, fallopian tube, or colorectal cancer increases the likelihood of developing ovarian cancer. Women who have used birth control have a decreased chance of developing ovarian cancer, whereas those who have taken fertility drugs may face an increased risk. Similarly, women who have experienced pregnancy and breastfeeding may face a reduced risk, while those who have never been pregnant have a higher risk. Ovarian cancer is predominantly seen in elderly women, being more likely to occur post-menopause[14].

Pathology:

Major Histopathologic Categories of Ovarian Cancer

1. **Epithelial**

Serous, mucinous, endometrioid, clear cell, transitional cell (Brenner), undifferentiated

2. **Germ Cell**

Dysgerminoma, endodermal sinus tumor, teratoma (immature, mature, specialized), embryonal carcinoma, choriocarcinoma, gonadoblastoma, mixed germ cell, polyembryona

3. **Sex Cord and Stromal**

Granulosa cell tumor, bibroma, thecoma Sertoli-Leydig cell, gynandroblastoma.

4. **Neoplasms Metastatic to the Ovary**

Breast, colon, stomach, endometrium, lymphoma[15].

Types and Characteristics:

Ovarian cancer typically originates from three types of tissue: about 85 to 95 percent from epithelial cells, 5 to 8 percent from stromal cells, and 3 to 5 percent from germ cells[16]. The kind of ovarian tumor differs based on the age of the person (Table 1). Epithelial cell tumors typically manifest in females over the age of 50. Stromal cell tumors can develop in females of all age groups, with some tumors like androblastomas being more prevalent during adolescence. Most often, germ cell tumors are found in patients under one year old and those between the ages of 15 and 19[17].

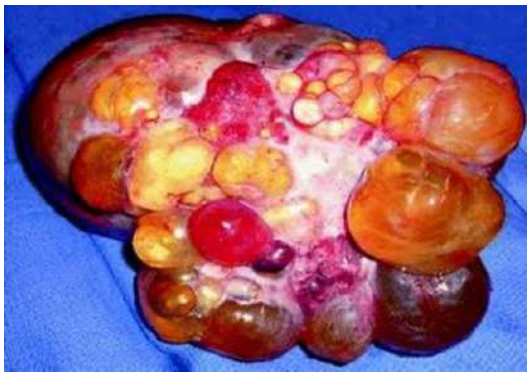


Fig. 1 Epithelial ovarian cancer.

Table. 1- Types and Characteristics[16,18]

Cancer type	Percentage of all ovarian cancers	Characteristics
Epithelial cell	85 to 95	Frequently seen in individuals over 50 years old; 15 percent of ovarian cancers involving epithelial cells are borderline or have low malignant potential, with a 10-year survival rate of up to 99 percent for stage I.

Serous		40 percent of all ovarian cancers; most common ovarian cancer
Endometrioid		20 percent of all ovarian cancers; 15 percent of endometrioid carcinomas coexist with endometriosis; 40 percent bilateral
Mucinous		Origin of 25 percent of ovarian cancers is unknown; could be linked to endometriosis; connected to pseudomyxoma peritonei.
Stromal cell	5 to 8	Derived from the sex cord of embryonic gonads
Granulosa-theca		A broad age range; can cause early sexual development in young girls; linked to conditions like endometrial hyperplasia, breast cystic disease, and endometrial cancer in adults; ascites present in 40% of fibromathecoma tumors; may also be associated with ascites and hydrothorax (Meigs syndrome).
Sertoil-leydig (androblastomas)		Common in adolescence; may be masculinizing; may block normal female sexual development
Germ cell	3 to 5	Found mostly in children and young adults 20 to 30 years of age; highly malignant; usually unilateral
Endodermal sinus tumor		Most common germ cell ovarian cancer in children; usually larger than 15 cm; median age of patients is 18 years, one third of patients are premenarchal
Embryonal (multipotential)		Extraembryonic: yolk sac carcinoma
		Primitive: embryonal carcinoma (highly malignant), precocious Puberty Somatic: immature teratoma Trophoblast: choriocarcinomas
		Undifferentiated: dysgerminomas (most common malignant germ cell ovarian cancer), 10 to 20 percent bilateral, radiosensitive
Mature		Mostly benign, dermoid cysts
Metastasis to ovaries	5 percent	Typically from breast or gastrointestinal primary sites

Symptoms:

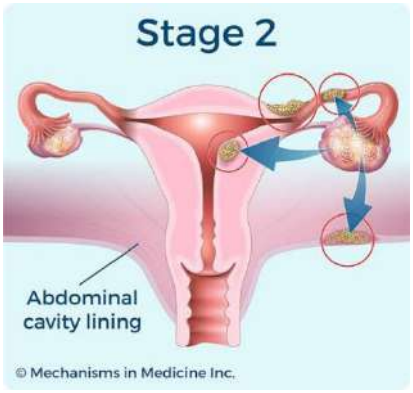
- Often vague and nonspecific lower abdominal pain/discomfort
- Feeling bloated, anorexia, pain abdomen/pelvis
- Frequency/urgency of urination.
- Ovarian cancer may found by chance during surgery for other cause or tests.
- Pain in the pelvis
- Pain on the lower side of the body
- Back pain
- Indigestion or heartburn
- More frequent and urgent urination
- Pain during sexual intercourse
- Nausea, Weight loss, Breathlessness, Fatigue (tiredness)
- Loss of appetite[15].
- Ovarian cancer is often referred to as a "silent killer" because it typically shows no noticeable signs or symptoms until the disease has progressed significantly.
- Actually, patients are often symptomatic for several months before the diagnosis, even with early-stage disease
- The difficulty is in distinguishing these symptoms from those that occur normally in

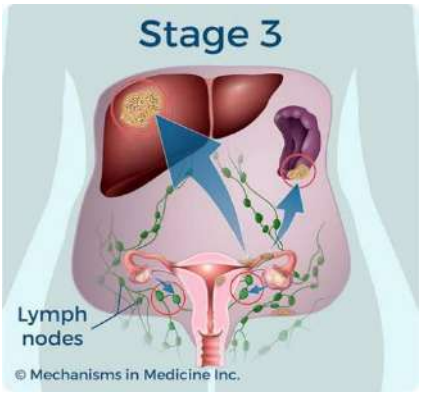
women or other diseases makes the diagnosis challenging.

- Increased abdominal size,
- Urinary urgency, and pelvic pain are reported.
- Abnormal vaginal bleeding occurs rarely.

Regrettably, many women and medical professionals often blame symptoms like these on menopause, getting older, changes in diet, stress, sadness, or issues with the bowels. Therefore, it is common for individuals to wait weeks or months before seeking medical advice or undergoing diagnostic tests[19].

Stages[20].





Screening:

The CA 125 test is not effective for screening ovarian cancer as it does not exclude the possibility of the disease, and a false positive result can trigger unnecessary invasive procedures. The USPSTF advises not to routinely screen for ovarian cancer[21]. The USPSTF does not recommend routine referral for genetic counseling or routine BRCA testing for women without a family history indicating a higher risk of BRCA1 or BRCA2 mutations. The USPSTF suggests referring women with a family history linked to higher risk of BRCA1 or BRCA2 mutations for genetic counseling and assessment for BRCA testing[22]. The majority of ovarian cancers that are passed down genetically (>90%) are caused by mutations in the BRCA1 or BRCA2 genes (autosomal dominant). Women with a personal history of both breast and ovarian cancer, ovarian cancer and a close relative with breast cancer under 50, or breast cancer under 50 and a close relative with ovarian cancer, or a close relative with a known BRCA1/BRCA2 gene mutation have a 20-25% chance of having genetic predisposition and should seek genetic risk assessment[23].

Diagnosis:

CA 125 levels are increased in numerous benign and malignant conditions, making it unhelpful in distinguishing ovarian cancer. Nevertheless, its usefulness in pre-operative assessment of pelvic masses can be valuable. Out of 854 patients with a pelvic mass, 343 patients (40%) displayed

elevated CA 125 levels exceeding 35 U/mL. Out of those with a raised CA 125, 130 individuals (38%) were found to have epithelial ovarian cancer, while 56 (16%) had a different type of cancer, and eight (2%) had a borderline ovarian tumor. When CA 125 and CASA were used together at certain levels to identify all benign patients as true negatives, a sensitivity of 69% was achieved. Ultrasound findings: several cysts, presence of solid areas, signs of spreading cancer, lesions on both sides, and ascites indicate a scoring of M = 1 for premenopausal individuals, and M = 2 for postmenopausal individuals. An index higher than 190 accurately predicted malignancy with a sensitivity of 85·4% and specificity of 98%[24].

Ovarian cancer usually emerges slowly with minimal warning signs or symptoms. Many ovarian tumors do not show symptoms until they have spread extensively in the abdominal area. A frequent occurrence of non-specific gastrointestinal issues, such as nausea, indigestion, and changes in bowel movements, is prevalent. Abdominal swelling due to accumulation of fluid in the abdomen is usually a sign of a severe illness. Occasionally, changes in bowel habits like constipation and reduced stool size are observed. Big tumors can create a feeling of heaviness or pressure in the pelvic area. Occasionally, an ovarian tumor can get trapped in the cul-de-sac and result in intense pain, difficulty with urination, discomfort in the rectum, and obstruction of the bowel. Up to 15% of women of reproductive age with an ovarian tumor may experience menstrual irregularities. Patients with ovarian cancer may experience vaginal bleeding due to either a synchronous endometrial carcinoma or metastatic disease in the lower genital tract. Ovarian stromal hyperplasia or hyperthecosis can also be linked to increased androgen production, leading to changes in the regular menstrual cycle[15].

Treatment:

Traditional treatment for ovarian cancer involves removing as much of the tumor as possible through surgery followed by a mix of platinum and nonplatinum chemotherapy, like carboplatin (formerly known as Paraplatin) and paclitaxel (also known as Taxol). There is no solid proof that undergoing chemotherapy before debulking surgery is better than traditional treatment for advanced epithelial ovarian cancer in women[25]. If the patient has had a thorough surgical staging procedure before, they can only be monitored. If staging is not finished and there are invasive implants, the patient may be either monitored or treated as EOC. If there is still disease present after the initial procedure, full surgery should be performed if fertility is not wanted, or a comprehensive surgery that preserves fertility should be done. Follow-up should occur every 3 to 6 months for a duration of up to 5 years, followed by yearly check-ups. During every visit, a physical examination that includes a pelvic examination should be conducted. If CA125 or any other tumor marker was previously elevated, it should be checked at every appointment. Surgical completion should be done after finishing having children in patients who had undergone unilateral salpingo-oophorectomy. Full blood count (FBC), Blood chemistry profile, and ultrasound are recommended for patients undergoing fertility-preserving surgery. In case of relapse, it is recommended to undergo surgical evaluation and debulking surgery [26]. Surgery: Generally, the treatment consists of removing the ovaries, fallopian tubes, uterus, nearby lymph nodes, and a fatty abdominal tissue fold (omentum) where ovarian cancer commonly spreads. Your surgeon will also extract the maximum amount of cancer from your abdominal area. If your ovarian cancer was caught in its initial stages, it may be feasible to have a less invasive surgery. Surgery for stage I ovarian cancer in women may entail the removal of one ovary and its accompanying fallopian tube.

This process could maintain the capacity to conceive offspring[27]. Chemotherapy: Following the surgical procedure, you will probably undergo chemotherapy in order to eliminate any cancer cells that may still be present. Chemotherapy medications can be administered through an IV or directly into the abdomen, or a combination of both methods. Chemotherapy could be the first option for treating advanced ovarian cancer in certain women[27].

Preventions:

Although there is currently no means to prevent ovarian cancer, the following factors have been linked to a reduced risk of developing ovarian cancer:

- Usage of birth control pills for more than five years.
- Breastfeeding.
- Giving birth.
- Having surgeries like hysterectomy, tubal ligation, or bilateral oophorectomy (removal of both ovaries)[28].
- Factors that decrease risk include hormonal birth control, tubal ligation, and breast feeding.
- Individuals who have a high genetic susceptibility to ovarian cancer may contemplate undergoing a procedure to remove their ovaries as a proactive step.
- This is often done after completion of childbearing years.
- This lowers the likelihood of developing breast cancer (by about 50%) and ovarian cancer (by approximately 96%) in individuals with a high risk.
- However, these statistics may overestimate the risk reduction because of how they have been studied[27].

For women who are at a high risk of ovarian cancer and decide against having prophylactic BSO, the National. NCCN currently suggests transvaginal ultrasonography and CA 125 measurement every six months between days 1 and 10 of the menstrual cycle. It should start at 35 years old, or five to 10 years before the youngest age at which ovarian cancer was diagnosed in the family[29].

CONCLUSION:

The therapy should involve thorough evaluation of cancer and pregnancy risks, a defined decision-making process for both the mother and the baby, the suitable treatment, and close monitoring post-treatment. Surgical staging is necessary for all suspected early-stage diseases, involving either unilateral oophorectomy or unilateral adenectomy, along with appropriate staging procedures if feasible. Surgery can be scheduled after 16 weeks of pregnancy to reduce the risk of miscarriage, and chemotherapy can start from the second trimester like in women who are not pregnant. Decisions regarding additional imaging like MRI or treatment plans are based on a mix of clinical symptoms, worrisome ultrasound findings, and increased tumor markers. In our situation, the choice to proceed with surgery was made during the MDT meeting. In conclusion, it is essential to have a team of specialists including an oncologist, obstetrician, and neonatologist for prompt management of early-stage ovarian carcinoma identified during pregnancy.

REFERENCES

1. Mok SC, Kwong J, Welch WR, Samimi G, Ozbun L, et al. Etiology and pathogenesis of epithelial ovarian cancer. Dis Markers 2007; 23(5–6): 367–376. doi: 10.1155/2007/474320.
2. Sankarnarayanan R, Ferlay J. Worldwide burden of gynaecological cancer: the size of the problem. Best Pract Res Clin Obstet Gynecol. 2006;20:207.
3. Howlader N, Noone AM, Krapcho M, et al. SEER cancer statistics review, 1975-2012, based on November 2014 SEER Data submission, posted to the SEER website,

April 2015. Bethesda.MD. National Cancer Institute; 2015. Available at http://seer.cancer,gov/csr/1975, 2012/.

4. Hoffman BL, Scorge JO, Schaffer JI, Halvorson LM, Bradshaw KD, Cunningham FG. Epithelial ovarian cancer, chapter-35. In: Williams Gynecology, 2nd edn, McGraw Hill Medical. New York; 2012.pp.853- 78.
5. A. Toss et al., "Hereditary ovarian cancer: Not only BRCA 1 and 2 Genes," BioMed Research International, vol. 2015. 2015.
6. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.
7. Palmer J, Vatish M, Tidy J. Epithelial ovarian cancer in pregnancy: a review of the literature. BJOG: an international journal of obstetrics and gynaecology. 2009; 116: 480-491.
8. Negri E, Franceschi S, Tzonou A, Booth M, La Vecchia C, et al. Pooled analysis of 3 European case-control studies: I. Reproductive factors and risk of epithelial ovarian cancer. Int J Cancer 1991; 49(1): 50–56. doi: 10.1002/ijc. 2910490110.
9. https://www.slideshare.net/slideshow/ovarian-cancer-66839372/66839372
10. Morch LS, Lokkegaard E, Andreasen AH, et al. Hormone therapy and different ovarian cancers: a National Cohort study. Am J Epidemiol. 2012;175:1234-42.
11. Fathalla MF. Incessant ovulation–a factor in ovarian neoplasia? Lancet. 1971;2(7716):163. doi:10.1016/S0140-6736(71)92335-X.
12. Risch HA, Marrett LD, Jain M, Howe GR. Differences in risk factors for epithelial ovarian cancer by histologic type: results of a case-control study. Am J Epidemiol. 1996;144(4):363–372.
13. Lancaster JM, Powell CB, Chen LM, et al. Society of Gynecologic Oncology statement on risk assessment for inherited gynaecologic cancer predispositions. Gynecol Oncol. 2015;136:3-7.
14. https://www.slideshare.net/slideshow/ovarian-cancer-232250416/232250416
15. https://www.slideshare.net/slideshow/ovarian-cancer-66839372/66839372
16. Young RH, Clement PB, Scully RE. The ovary. In: Sternberg SS, Antonioli DA, Mills SE, Carter D, Oberman HA, eds. Diagnostic Surgical Pathology. 2nd ed. New York, NY: Raven Press; 1994.
17. Centers for Disease Control and Prevention United States cancer statistics: 1999-2005 cancer incidence and mortality data U.S. Department of Health and Human Services. http://www.cdc.gov/uscs. Accessed February 26, 2009.
18. Crum CP. The female genital tract In: Kumar V, Fausto N, Abbas AK, eds. Robbins and Cotran Pathologic Basis of Disease. 7th ed. Philadephia, Pa: Elsevier Inc; 2005.
19. https://www.slideshare.net/slideshow/ovarian-tumors-48053706/48053706
20. https://ovarian.org/about-ovarian-cancer/types-and-stages/
21. U.S. Preventive Services Task Force. Screening for ovarian cancer: recommendation statement. U.S. Preventive Services Task Force. Am Fam Physician. 2005;71(4):759-762.
22. U.S. Preventive Services Task Force. Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement [published correction in Ann Intern Med. 2005;143(7):547]. Ann Intern Med. 2005;143(5):355-361.
23. Hoffman BL, Scorge JO, Schaffer JI, Halvorson LM, Bradshaw KD, Cunningham

FG. Epithelial ovarian cancer, chapter-35. In: Williams Gynecology, 2nd edn, McGraw Hill Medical. New York; 2012.pp.853-78.

24. McGuckin MA, Ramm LE, Joy GJ, Free GJ, Ward KE, Ward BG. Preoperative discrimination between ovarian carcinoma, non-ovarian gynecological malignancy and benign adnexal masses using serum levels of CA 125 and the-polymorphic epithelial mucin antigens CASA, OSA, and MSA. Int] Gynecol Cancer 1992; 2: 119-28
25. Morrison J, Swanton A, Collins S, Kehoe S. Chemotherapy versus surgery for initial treatment in advanced ovarian epithelial cancer. Cochrane Database Syst Rev. 2007;(4):CD005343.
26. NCCN Clinical Practice Guidelines in Oncology, Ovarian Cancer. 2015. available at www.nccn.org.
27. https://www.slideshare.net/slideshow/ovarian-cancer-86281960/86281960
28. https://www.pacehospital.com/world-ovarian-cancer-day
29. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Genetic/familial high-risk assessment: breast and ovarian. V.I. 2008. http://www.nccn.org/professionals/physician_gls/PDF/genetics_screening.pdf (subscription required). Accessed March 2, 2009.

HOW TO CITE: Rutuja Shingare*, Bhanage Pratik, Dr. Megha Salve, A Review Article On: Ovarian Cancer, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 11, 1112-1120. https://doi.org/10.5281/zenodo.14210652