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An Overview on Gynaecological Cancers

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ABSTRACT

Gynaecological cancers represent a significant public health issue, especially for women, ranking among the most common cancer forms. In developing nations like India, these cancers pose serious challenges due to factors such as limited cancer awareness, diverse pathological presentations, and restricted access to proper screening facilities. Consequently, many women in India are diagnosed at advanced disease stages, leading to poor prognosis and outcomes.

The main types of gynaecological cancers include:

Ovarian cancer

Endometrial (uterine) cancer

Cervical cancer

Vaginal cancer

Vulvar cancer

Among these, ovarian cancer has become a significant malignancy in Indian women, with rising incidence over the years. Although cervical cancer has declined, it remains the second most common cancer in women after breast cancer.

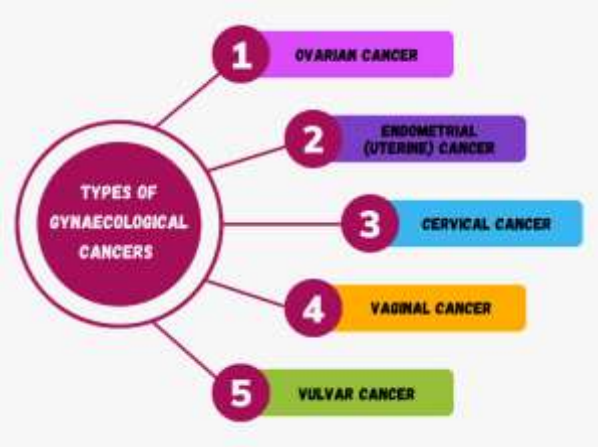
Indian researchers have made notable advancements in gynaecologic oncology, contributing valuable data across domains such as basic science, preventive strategies, pathology, radiological imaging, and clinical outcomes. These studies have enhanced our understanding of these cancers and provided crucial insights into demographics and survival rates within the Indian population.

This review summarises and discusses key studies conducted in India on all types of gynaecological cancers.

KEY WORDS: - Gynaecological cancer, types of Gynaecological cancer, women health, symptoms, diagnosis, treatments, prevention.

1. Introduction.

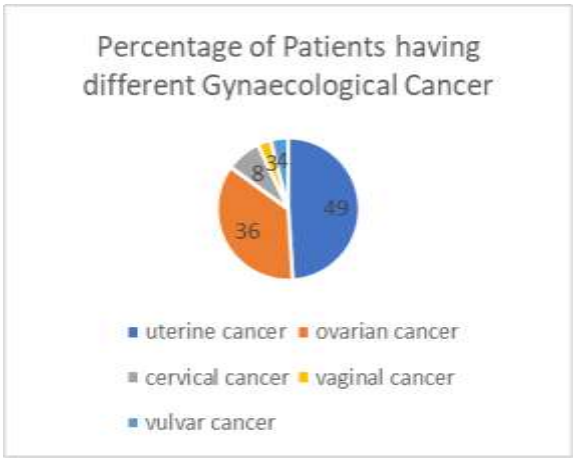
Gynaecological cancers encompass a group of malignancies that affect a woman's reproductive organs. These cancers arise in the tissues of the female reproductive system, which includes the cervix, ovaries, uterus, vagina, and vulva. Each type of gynaecological cancer is distinct, with unique risk factors, symptoms, and treatment options.



{Fig. 1.1 Types of gynaecological cancer}

Among these, ovarian and cervical cancers are the most prevalent, affecting women both globally and in India. While the rate of cervical cancer cases has been decreasing., it remains the second most common cancer in women after breast cancer. In India, an estimated 122,844 women are diagnosed with cervical cancer annually, with 67,477 deaths attributed to the disease. Over the years, Indian researchers have made significant contributions to gynaecologic oncology, and this review aims to highlight key studies in the field. It examines various aspects of each type of gynaecological cancer, focusing on demographics, clinical outcomes, and survival rates within the Indian population.

In the United States, gynaecological cancers affect more than 95,000 women each year, leading to over 30,000 deaths. These cancers include those of the ovaries, uterus, cervix, vagina, and vulva. Uterine cancer is the most frequently diagnosed, but ovarian cancer remains the deadliest due to challenges in early detection. In research, the percentage of patients having different types of gynaecological cancer is found as follows:



{Fig. 1.2 percentage of patients having different types of gynaecological cancer}

Early detection and prevention strategies, such as regular screenings, HPV vaccination, and increased awareness of symptoms, are crucial for managing and reducing the burden of gynaecological cancers. Treatment options depend on the type and stage of cancer and may involve surgery, radiation therapy, chemotherapy, targeted therapy, or a combination of these. Advances in medical research and technology continue to improve outcomes and enhance the quality of life for women diagnosed with these cancers.

2. Types of Gynaecological Cancer

2.1 Ovarian Cancer

Significant progress has been made in understanding the behaviour and underlying causes of the various types of ovarian cancer, with several studies by Indian researchers contributing to this field. One notable study by Basu and colleagues investigated the role of the transforming growth factor-beta (TGF-β) signalling pathway in human ovarian tissues using immunohistochemistry (IHC). Their research found that the TGF-β pathway, activated by the pituitary homeobox 2 (PITX2), regulates genes associated with cell invasion, such as SNAI1, CDH1, and MMP9 ($P < 0.01$), all of which play a crucial role in enhancing the motility and invasiveness of ovarian cancer cells. The study highlighted SNAI1 and MMP9 as key mediators in PITX2-driven invasiveness. Overexpression of PITX2 was shown to decrease epithelial markers ($P < 0.01$) and increase mesenchymal markers ($P < 0.01$), both of which contribute significantly to ovarian cancer progression.

Ovarian cancer remains a significant public health issue in India. According to recent estimates, approximately 45,000 to 50,000 new cases are diagnosed annually, making it one of the leading causes of cancer-related deaths among women in the country. However, promising data indicate that there has been a 29% decline in the overall incidence of ovarian cancer between 1985 and 2014. Experts suggest that this decrease is largely due to the increased use of oral contraceptives, which have been shown to reduce the overall risk of ovarian cancer when taken for five to nine years.

2.1.1 Risk Factors

Various factors raise a woman's likelihood of developing ovarian cancer, with the most notable being mutations in the BRCA1 or BRCA2 genes. Research indicates that women with these mutations have approximately a 30% risk of developing ovarian cancer after the age of 70. Other significant risk factors include:

1. **Genetic Factors**: Women of Ashkenazi Jewish descent are more likely to have mutations in the BRCA genes.
2. **Obesity**: Being overweight can cause hormonal imbalances, which may raise the risk of ovarian cancer.
3. **Personal or Family History** A background of breast, uterine, or colorectal cancer, as well as conditions like endometriosis, raises the risk.
4. **Reproductive Factors:** Women who haven't had children or who have trouble getting pregnant are at a greater risk. The risk also grows as they get older, particularly after middle age.

2.1.2 Symptoms

The symptoms of ovarian cancer are often vague and can be mistaken for other common health issues. However, it is important to consult a doctor if any of the following symptoms persist:

1. Pelvic or Abdominal Pain: This may feel like cramping or a constant, dull ache.

2. Bloating or Difficulty Eating: Feeling full quickly or persistent bloating may be related to fluid buildup or a growing tumour.

a. **Frequent Urination**: A tumour pressing on the bladder can cause frequent or urgent urination.

b. **Unusual Vaginal Discharge**: Any abnormal discharge, particularly post-menopausal bleeding, should be evaluated as it could signal ovarian cancer.

2.1.3 Diagnosis

Unfortunately, there is currently no effective screening test for ovarian cancer. However, the following diagnostic methods may be used if cancer is suspected:

1. **Pelvic Exam**: This exam allows a doctor to check the size, shape, and position of the ovaries and uterus. Further tests such as ultrasounds or biopsies may be recommended if abnormalities are found.
2. **CA-125 Blood Test**: The CA-125 blood test checks the level of cancer antigen 125 protein, which can be higher in women with ovarian cancer. However, elevated levels can also be caused by non-cancerous conditions like endometriosis, so this test is not used for routine screening but as a component of a larger diagnostic approach.

2.1.4 Treatment for Ovarian Cancer

Ovarian cancer treatment generally includes a mix of therapies, based on the disease stage, the patient's overall health, and other considerations. Common treatments include:

1. **Surgery**: The primary treatment is an operation to take out the tumour. This may include:
2. **Oophorectomy**: Removal of one or both ovaries.
3. **Hysterectomy**: Removal of the uterus and sometimes the cervix.
4. **Debulking Surgery**: Reducing tumour size to improve the effectiveness of other treatments.
5. **Chemotherapy**: Drugs like carboplatin and paclitaxel are used to kill cancer cells, typically after surgery, to target any remaining cancer.
6. **Targeted Therapy**: This approach uses drugs that specifically attack cancer cells, such as PARP inhibitors, which are particularly effective for patients with BRCA mutations.
7. **Hormone Therapy**: Used when cancer is hormone-sensitive, this treatment blocks or interferes with hormone production.
8. **Radiation Therapy**: Less common for ovarian cancer, but it may be used in cases where the cancer has spread.
9. **Immunotherapy**: A novel therapy that employs the body's immune system to battle cancer.
10. **Clinical Trials**: Patients may also participate in clinical trials that offer access to new and experimental treatments.

2.1.5 Prevention Strategies

Even though there isn't a guaranteed way to prevent ovarian cancer, several approaches can help decrease the risk:

1. **Oral Contraceptives** Extended use of birth control pills has been found to considerably reduce the risk of ovarian cancer.
2. **Pregnancy and Breastfeeding**: Women who have had at least one full-term pregnancy, especially before age 35, and those who breastfeed may have a reduced risk.
3. **Surgical Interventions**: Procedures like tubal ligation or prophylactic oophorectomy for women with BRCA mutations can reduce risk.
4. **Healthy Lifestyle:** Following a nutritious diet, engaging in regular physical activity, and avoiding smoking can lower the risk of ovarian cancer.
5. **Genetic Counselling**: Women who have a family history of ovarian or breast cancer should consider genetic counselling and BRCA testing to assess their risk and explore preventive options.

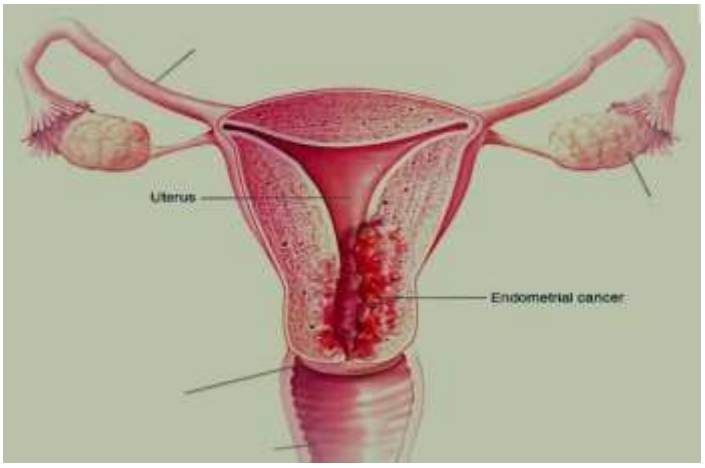
2.1.6 Advanced New Treatments

Recent progress in ovarian cancer treatment brings new hope. PARP inhibitors, like olaparib, block cancer cells from repairing their DNA, particularly benefiting women with BRCA mutations. Other promising therapies include monoclonal antibodies that target specific cancer cells and the combination of dendritic cell vaccines with immunotherapy drugs like pembrolizumab, which aim to prevent cancer recurrence in advanced stages.

2.2 Uterine/Endometrial Cancer

Endometrial cancer, commonly referred to as, **uterine cancer**, is the most frequently occurring gynaecological cancer in Western countries. In India, however, the incidence rates are relatively low. When diagnosed, in India, endometrial cancer frequently appears at an early stage. which typically leads to a favourable outcome and better prognosis for patients.

Endometrial cancer begins in the **endometrium**, the lining of the uterus. This cancer typically develops over time, progressing from benign cellular changes to precancerous conditions and eventually cancerous tumours. Various factors, including genetic mutations and hormonal imbalances, play significant roles in its initiation and progression.



2.2.1 Factors Influencing Development

1. Hormonal Factors: Prolonged exposure to high levels of **oestrogen** increases the chance of developing endometrial cancer and can be affected by factors like obesity, hormone replacement therapy (HRT), or particular medical conditions that result in an oestrogen-dominant environment.

2. Genetic Predisposition: Inherited genetic mutations, such as those linked to **Lynch syndrome**, significantly increase the risk of endometrial cancer. This syndrome involves mutations in DNA mismatch repair genes and elevates the chances of several cancers, including endometrial and colorectal cancers.

3. Lifestyle and Health Conditions: Obesity, diabetes, and hypertension are important risk factors. These conditions are often linked to hormonal imbalances that contribute to the development of cancer.

2.2.2 Risk Factors

Multiple factors contribute to a higher risk of developing endometrial cancer:

1. **Hormonal Imbalances**: Conditions that increase oestrogen levels, such as **polycystic ovary syndrome (PCOS)**, obesity, or the use of Hormone replacement therapy that does not include progesterone is associated with an increased risk of endometrial cancer.
2. **Age**: The most cases are found in women aged over 50, especially after menopause.
3. **Family History**: A family history of cancers, such as endometrial, ovarian, or breast cancer, elevates the risk.
4. **Genetic Mutations**: Hereditary conditions like **Lynch syndrome** increase susceptibility to endometrial cancer.
5. **Diabetes and Hypertension**: Both conditions are linked to an increased risk of developing endometrial cancer.
6. **Never Been Pregnant**: Women who have never been pregnant have an elevated risk, likely due to prolonged exposure to unopposed oestrogen throughout their reproductive lives.

2.2.3 Symptoms

Common symptoms of endometrial cancer include:

1. **Abnormal Vaginal Bleeding [metrorrhagia]**: This can include bleeding between menstrual cycles or postmenopausal bleeding, which is a key warning sign.
2. **Pelvic Pain**: Persistent pain or discomfort in the pelvic region.
3. **Abnormal Vaginal Discharge**: This discharge may be watery, bloody, or pink.
4. **Pain During Intercourse**: Pain experienced during sexual activity.
5. **Unexplained Weight Loss**: Significant weight loss without an identifiable cause.

2.2.4 Diagnosis

Endometrial cancer is diagnosed through various methods:

1. **Pelvic Examination**: A physician examines the pelvic region to identify abnormalities. A pelvic examination is an essential component of diagnosing uterine cancer. In this exam, a healthcare provider evaluates the pelvic area, which encompasses the uterus, ovaries, fallopian tubes, and nearby tissues. The pelvic exam typically works on Preparation, External examination, speculum insertion, internal examination, assessment of symptoms and follow-up.

In summary, a pelvic examination is an important method for early detection and diagnosis, allowing healthcare providers to recognize problems that may need additional investigation or treatment.

2. **Ultrasound**: Ultrasound is a widely used imaging technique for diagnosing and evaluating uterine cancer. It is non-invasive and provides detailed insights into the uterus's structure.
3. **Transabdominal Ultrasound**: This method offers a broad view of the uterus by scanning through the abdominal wall.
4. **Transvaginal Ultrasound**: A more detailed approach A probe is inserted into the vagina to provide clearer images of the uterus, helping to identify any abnormalities, such as thickened uterine lining, masses, or tumours.
5. **Endometrial Biopsy**: A tiny sample of endometrial tissue is extracted and examined under a microscope for cancerous cells. It is a crucial diagnostic tool, especially in women with abnormal uterine bleeding or postmenopausal bleeding.
6. **Curettage and Dilation (C&D)**: A minor surgical procedure used to scrape a tissue sample from the uterus for further examination. It is particularly helpful when previous diagnostic tests are inconclusive.

2.2.5 Treatment

The treatment plan for endometrial cancer is based on the stage of the cancer, the overall health of the patient, and other individual factors. Common treatments include:

1. **Surgery**: The primary treatment for most patients is surgery, often involving a **hysterectomy** (removal of the uterus or uterus removal process). In some cases, the ovaries and fallopian tubes may also be removed to reduce the risk of cancer spread.
2. **Radiation Therapy**: Radiation uses high-energy rays to kill cancer cells or shrink tumours. It is often used after surgery if the cancer has spread beyond the uterus.
3. **Chemotherapy**: Chemotherapy uses drugs to kill cancer cells and is often employed when cancer has spread to other parts of the body.
4. **Hormone Therapy**: Some hormone-sensitive types of endometrial cancer may respond to hormone therapy, which aims to block hormones, like oestrogen, that fuel cancer growth.
5. **Targeted Therapy**: Advanced therapies like **targeted drugs** focus on specific molecular mechanisms in cancer cells. These drugs are especially helpful in treating advanced or recurrent cases of endometrial cancer.
6. **Immunotherapy**: **Dostarlimab**, an immune checkpoint inhibitor approved in 2023, it is now combined with chemotherapy to treat advanced or recurrent endometrial cancer in patients with **mismatch repair deficiency (dMMR)**. This drug has demonstrated encouraging results in slowing disease progression.
7. **Combination Therapies**: **Pembrolizumab** (an immune checkpoint inhibitor) combined with **Lenvatinib** (a targeted therapy) has demonstrated effectiveness in treating advanced cases of uterine cancer, especially those with **microsatellite instability-high (MSI-H)** tumours.

2.2.6 Prognosis

The prognosis of endometrial cancer largely depends on the stage at which the cancer is detected. Early-stage cancers, which are confined to the uterus, tend to have better survival rates compared to more advanced cases where the cancer has spread. **Early detection** through regular medical check-ups and prompt treatment improves outcomes for patients.

Overall, advancements in treatment options, such as targeted therapies, immunotherapies, and combination approaches, are providing more personalized and effective treatments, enhancing the potential for better outcomes, even in progressive stages of the disease.

2.2.7 Vaccinations

Currently there is currently no vaccine that specifically prevents uterine (endometrial) cancer. However, vaccines targeting human papillomavirus (HPV) help lower the risk of certain gynaecological cancers, such as cervical cancer, which can influence overall uterine health. While HPV is not directly linked to endometrial cancer, it is a primary cause of the majority of cervical cancers., it is a major cause of most cervical cancers, and vaccines like Gardasil and Cervarix protect against HPV infections.

Here's an overview of vaccines relevant to uterine and other gynaecological cancers:

1. **HPV Vaccines (Gardasil, Gardasil 9, Cervarix)**:

Purpose: These vaccines primarily prevent cancers such as cervical, vaginal, vulvar, and anal cancers resulting from high-risk HPV types, such as HPV 16 and 18. They may also reduce the chance of some oropharyngeal cancers.

Connection to Uterine Health: Although they does not directly prevent endometrial cancer, by reducing the threat of cervical cancer, HPV vaccines indirectly promote overall gynaecological health.

2. **Therapeutic Vaccines (In Development)**:

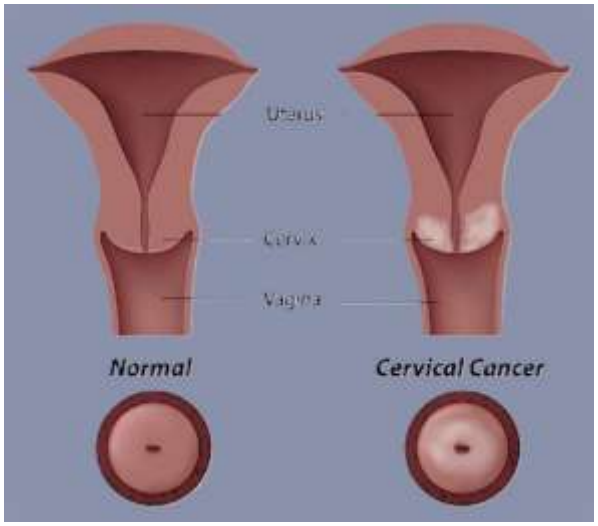
Experimental vaccines to treat cancers, including uterine cancer, are currently being researched. These vaccines aim to enhance the immune system's ability to attack existing cancer cells but are still in clinical trials and are not yet widely available.

While HPV vaccines contribute to general gynaecological health, uterine cancer itself is generally linked to other factors, including hormonal imbalances, obesity, and age, which are not currently preventable through vaccination.

2.3 Cervical Cancer

Cervical cancer is mainly caused by a long-term infection with high-risk strains of the human papillomavirus (HPV), particularly HPV types 16 and 18 The oncoproteins E6 and E7 produced by HPV interfere with normal cellular functions in the cervix, resulting in abnormal cell growth and cancer. The cancer originates in the cervical epithelium and can advance from pre-invasive stages, referred to as cervical intraepithelial neoplasia (CIN), to invasive cancer if not treated. CIN is categorized into different stages (CIN1 to CIN3) depending on the depth of abnormal cell involvement, with CIN3 representing the most progressive pre-invasive stage.

Cervical Cancer can be categorized into two main types: squamous cell carcinoma, which is the most prevalent form, and **adenocarcinoma**, which arises from glandular epithelial cells. Both types share similar risk factors, including HPV infection, hormonal influences (such as high levels of progesterone and oestrogen), and immune system factors.



2.3.1 Risk Factors for Cervical Cancer

1. **HPV Infection**: HPV infection is the primary threating factor for cervical cancer, especially infections caused by high-risk HPV types such as 16 and 18.
2. **Smoking**: Smoking weakens the natural defence system, making it harder for the body to clear HPV infections, thus increasing cancer risk.
3. **Weakened Immune System**: Conditions that suppress the immune system, such as HIV/AIDS, greater susceptibility to cervical cancer and HPV infection.
4. **Sexual History**: Engaging in early sexual activity, having multiple sexual partners, or having a partner with a history of multiple sexual partners can raise the chance of acquiring HPV.
5. **Long-term Oral Contraceptive Use**: Extended use of birth control pills can increase the possibility of developing cervical cancer, particularly in those already infected with HPV.
6. **Multiple Pregnancies**: Having multiple full-term pregnancies may raise the greater probability of cervical cancer.
7. **Family History**: A family history of this type of cancer may point to inherited genetic susceptibilities.

8. **Exposure to DES**: Women whose mothers took the drug diethylstilbestrol (DES) during pregnancy are at an elevated risk for developing a rare form of cervical cancer.

2.3.2 Symptoms of Cervical Cancer

Cervical cancer often presents with no symptoms in its early stages. As the disease progresses, symptoms may include:

1. **Abnormal Vaginal Bleeding**: Abnormal vaginal bleeding can happen between menstrual periods, after menopause. or following sexual intercourse.
2. **Unusual Vaginal Discharge**: A watery, bloody, or foul-smelling discharge is often observed.
3. **Pelvic Pain**: Chronic pain in the lower abdominal region or pelvic area may indicate a problem.
4. **Pain During Intercourse**: Discomfort or ache during sexual activity/ intercourse.
5. **Urinary or Bowel Changes**: In advanced cases, changes in urinary or bowel habits may occur.

2.3.3 Diagnosis of Cervical Cancer

1. **Pap Test (Pap Smear)**: A screening test identifies abnormal cells in the cervix that could potentially develop into cancer. During a pelvic examination, cells are gathered from the cervix and examined for abnormalities. Abnormal results may require further testing.
2. **HPV Testing**: This test detects greater risk HPV types in cervical cells, helping determine if further investigation is needed. It is often recommended for women over 30 as part of routine screening.
3. **Colposcopy**: A colposcope is utilized to thoroughly inspect the cervix for abnormal areas that might not be seen during a regular pelvic examination. A special solution may be applied to highlight abnormal cells.
4. **Biopsy:** A biopsy is conducted to verify the existence of cancer. Small tissue samples are taken from the cervix for microscopic examination.
5. **Imaging Tests**: If cancer is diagnosed, imaging tests like CT scans, MRIs, or PET scans are done to determine the extent of cancer spread (staging).

2.3.4 Treatment of Cervical Cancer

Treatment options depend on the stage of the cancer and the patient's overall health.

1. **Surgery**:

Conization: Removes a cone-shaped piece of tissue from the cervical region.

Hysterectomy: Involves the removal of the uterus and cervix. A radical hysterectomy may be performed if the cancer is advanced.

Trachelectomy: Removes the cervix but preserves the uterus for women wishing to maintain fertility.

2. **Radiation Therapy**:

External Beam Radiation: High-energy rays target the cancer from outer side of the body.

Brachytherapy: Radioactive materials are placed near or inside the tumour to deliver targeted radiation.

3. **Chemotherapy**: Often used in combination with radiation, chemotherapy drugs like cisplatin and carboplatin are used to kill cancer cells or stop them from growing and dividing.
4. **Targeted Therapy**: Drugs like **bevacizumab** (Avastin) inhibit blood vessel growth in tumours, slowing cancer progression.
5. **Immunotherapy**:

Checkpoint Inhibitors: Drugs like **pembrolizumab** and **nivolumab** help the immune response system to identify and destroy cancer cells. These are particularly useful for recurrent or treatment-resistant cervical cancer.

Cancer Vaccines: Experimental vaccines are being developed to enhance the immune system's response to cancerous cells.

6. **Multidisciplinary Approach:** Treating vaginal cancer typically requires a team of healthcare professionals, including gynaecologic oncologists, radiation and medical oncologists, reconstructive surgeons, and palliative care professionals. This collaborative approach ensures that each patient receives a tailored treatment plan that not only focuses on controlling the cancer but also addresses symptom management and enhances overall health of person and their life satisfaction.

7. **Palliative Care:** Palliative care is essential for patients with advanced or recurrent vaginal cancer, as it helps relieve symptoms and enhances quality of life. This care includes managing pain, addressing issues such as bleeding or ulceration, and offering emotional support. By integrating consoling care with other treatments, patients can maintain comfort, dignity, and better manage the challenges associated with advanced disease.
8. **Clinical Trials:** Clinical trials are essential for progressing treatment options for vaginal cancer, particularly given its rarity. These studies explore new drug therapies, innovative surgical techniques, and combinations of chemotherapy and radiation. For patients with advanced or recurrent cancer, clinical trials can provide access to cutting-edge treatments that may not yet be widely available, offering hope for improved outcomes.

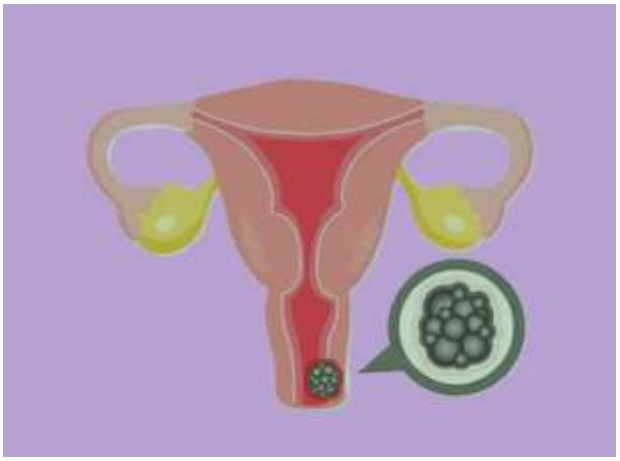
2.3.5 Prevention of Cervical Cancer

The essential factor in preventing cervical cancer is reducing HPV infection risk through vaccination, screening, and safe sexual practices. **HPV vaccines**, such as Gardasil and Cervarix, protect against high-risk HPV strains, significantly lowering the chances of cervical cancer. Regular Pap smears and HPV testing are necessaryfor early detection and successful treatment.

In conclusion, cervical cancer remains a significant health challenge, but with early detection, effective treatment options, and preventive measures like HPV vaccination, the impact of this disease can be greatly reduced.

2.4 Vaginal Cancer

Vaginal cancer is a rare type of cancer that affects the vagina, a muscular tube connecting the uterus to the external genitalia. Although human papillomavirus (HPV) is a leading cause, especially types 16 and 18, there are also non-HPV-related pathways that contribute to the expansion of this disease. Vaginal cancer can progress from vaginal intraepithelial neoplasia (VAIN), a less severe form, to non-invasive, and may eventually advance to invasive cancer, which is the most aggressive type.



2.4.1 Key Causes and Mechanisms

1. **HPV**: Similar to cervical cancer, HPV is strongly linked to vaginal cancer, particularly HPV types 16 and 18.
2. **Non-HPV Pathways**: Genetic mutations, like alterations in the TP53 gene, and exposure to radiation therapy can lead to vaginal cancer non-dependent of HPV.
3. **Other Precursors**: Conditions like atypical cervical ectropion and vaginal adenosis are sometimes linked to vaginal clear cell cancer.
4. **Hormonal Factors**: Vaginal oestrogen use post-menopause carries the same cancer risks as not using it, including breast, colorectal, and endometrial cancers.

2.4.2 Risk Factors

1. **HPV Infection**: Infection with high-risk HPV types (16, 18) is a major risk factor.
2. **Age**: Vaginal cancer is more common in women over 60.
3. **History of Cervical/Vulvar Cancer**: Previous cancers in these areas increase risk.
4. **Radiation Therapy**: Prior radiation to the pelvic area can increase risk.

5. **DES Exposure**: In-utero exposure to diethylstilbestrol (DES) greater the danger for clear cell adenocarcinoma.
6. **Smoking**: Particularly in women having HPV, smoking increases risk.
7. **Weakened Immune System**: Conditions like HIV/AIDS can elevate the risk.
8. **Long term Inflammation**: ongoing irritation in the vaginal area may lead to cancer development.

2.4.3 Symptoms

Vaginal cancer is often asymptomatic in early stages, but later symptoms can include:

1. Abnormal vaginal bleeding (between periods, post-menopause, or after intercourse).
2. Watery or blood-tinged vaginal discharge or spotting.
3. Pain during intercourse or sexual activity
4. Pelvic pain or discomfort.
5. Lump or mass in the vagina.
6. Painful urination(dysuria) or bowel habit changes (in advanced stages).

2.4.4 Diagnosis

Vaginal cancer diagnosis includes:

1. **Pelvic Exam**: Checks for lumps or abnormalities.
2. **Pap Test**: Primarily for cervical cancer, it may detect abnormal vaginal cells.
3. **Colposcopy**: A close-up examination of the vagina and cervix using a magnifying device.
4. **Biopsy**: Removes tissue samples for testing.
5. **Imaging Tests**: CT scans, MRIs, and PET scans help assess the extent of cancer spread.

2.4.5 Treatment: -

Treatment depends on the cancer stage, size, location, and patient health:

1. **Surgery**:

Laser Surgery: Removes precancerous or early-stage cancer.

Vaginectomy: Partial or complete separation of the vagina.

Radical Hysterectomy: Withdrawal of the uterus, cervix, part of the vagina, and surrounding tissues.

Pelvic Exenteration: Removes organs like the bladder or rectum if the cancer has spread extensively.

2. **Radiation Therapy and Chemotherapy**:

External Beam Radiation and **Brachytherapy** target cancer cells directly.

Chemotherapy is often combined with radiation for advanced cases.

3. **Targeted Therapy**: Drugs like trastuzumab deruxtecan deliver chemotherapy directly to cancer cells, limiting damage to healthy tissue.
4. **Immunotherapy**: Checkpoint inhibitors like pembrolizumab (Keytruda) boost the immune system's ability to fight against cancer, particularly in advanced cases.

2.4.6 Prevention:

Preventive measures include:

1. **HPV Vaccination**: Can protect the HPV-related cancers, including vaginal cancer.
2. **Regular Gynaecological Exams**: Routine pelvic examination and Pap smears help in detection of early-stage cancers or precancerous conditions.

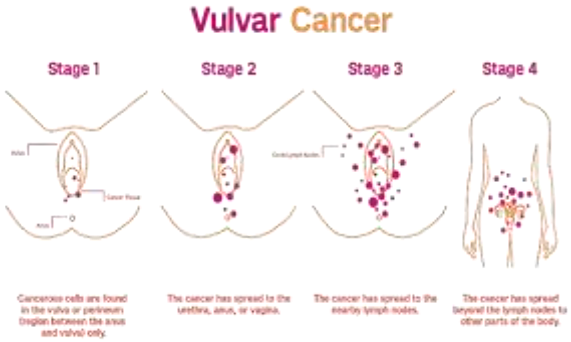
3. **Quit Smoking**: Reduces the risk of various cancers.
4. **Safe Sex Practices**: Using condoms and limiting sexual partners decreases the pitfall of HPV infection.
5. **Awareness of DES Exposure**: Women exposed to DES in utero should inform healthcare providers for monitoring.

2..4.7 Conclusion: -

Vaginal cancer is rare but serious. Early detection through regular screening and awareness of symptoms can improve treatment outcomes.

2.5 Vulvar Cancer

Vulvar cancer is a unique type of cancer that occurs on the outer surface of the female genitalia, known as the vulva. This cancer most frequently impacts the outer vaginal lips (labia majora), but it can also occur on the inner lips (labia minora), clitoris, or vaginal opening. Vulvar cancer typically develops slowly, recurrently from many years, and can be preceded by pre-cancerous changes called **vulvar intraepithelial neoplasia (VIN)**.



2.5.1 Mechanisms of Vulvar Cancer Development

Vulvar cancer develops through two primary mechanisms:

1. **Non-HPV-Related Pathway**: This involves the presence of conditions like **lichen sclerosis** and **differentiated vulvar intraepithelial neoplasia (dVIN)**. Around 80% of vulvar cancers arise through this pathway. Lesions of dVIN and vulvar squamous cell carcinomas share similar **TP53 mutations**, which are important in this cancer's development.
2. **HPV-Related Pathway**: This affects primarily younger women who have been infected with large imperil HPV strains, particularly **HPV 16**. The percentage of vulvar cancers caused by HPV varies widely, ranging from 15% to 79% across different populations.

Other contributing factors to vulvar cancer development include impaired DNA repair mechanisms, disruptions in cellular signalling pathways, and abnormalities in cell regulation cycle

2.5.2 Risk Factors for Vulvar Cancer

1. **Age**: Vulvar cancer is most common in women over aged60.
2. **HPV Infection**: Persistent infection with high-risk types of HPV, especially HPV 16 and 18, increases the hazard.
3. **Smoking**: Smoking weakens the immunity system and makes it harder to fight off infections like HPV, raising the venture of vulvar cancer.
4. **Weakened Immune System**: Women with conditions like HIV/AIDS or those on immunosuppressive medications are at higher risk.
5. **Chronic Vulvar Conditions**: Conditions like **lichen sclerosis**, which cause long-term irritation, inflammation and itching of the vulvar skin, can lead to cancer.
6. **History of Cervical Cancer**: A anterior past of these cancers increases the likelihood of developing vulvar cancer.
7. **Vulvar Intraepithelial Neoplasia (VIN)**: VIN is a pre-cancerous condition where abnormal cells appear on the vulva's surface and can progress to vulvar cancer if left untreated.

2.5.3 Symptoms of Vulvar Cancer

In its early stages, vulvar cancer may not cause noticeable symptoms. As it progresses, symptoms may include:

1. **Persistent Itching**: One of the most prevalent early indicators.
2. **Pain or Tenderness**: Discomfort or pain in the vulva, particularly during urination or sexual activity.
3. **Skin Changes**: Changes in vulvar skin colour or texture, including sores, lumps, or non-healing ulcers.
4. **Unusual Bleeding**: Bleeding not related to menstruation, including after sexual intercourse.
5. **Lumps or Growths**: Wart-like growths or lumps on the vulva.
6. **Thickened or Discoloured Skin**: The skin may appear thickened, rough, or whitish.

2.5.4 Diagnosis of Vulvar Cancer

To diagnose vulvar cancer, healthcare providers use several diagnostic methods:

1. **Pelvic Examination**: A thorough exam of the vulva, vagina, and cervix to check for abnormalities.
2. **Biopsy**: If abnormal areas are detected, a biopsy is performed to remove a tissue sample and check for cancer cells.
3. **Imaging Tests**: If cancer is confirmed, imaging tests such as CT scans, MRIs, or PET scans are used to determine the extent of the cancer and detect metastasis (cancer spread).

2.5.5 Treatment Options for Vulvar Cancer

Treatment depends on the stage of the cancer disease, the tumour's location, size and the patient's overall health. Common treatment options include:

1. **Surgery**:

Wide Local Excision: Removal of the cancerous tissue along with a margin of healthy tissue to ensure all cancer cells are eliminated.

Vulvectomy: Surgical removal of part or all of the vulva. This depends on the extent of the cancer.

Lymph Node Dissection: Removal of lymph nodes in the groin to inspect for cancer spread.

2. **Radiation Therapy**:

External Beam Radiation: High-energy rays from outer side of the body target cancer cells to destroy them.

Brachytherapy: Radioactive materials are kept inside or near the tumour for targeted treatment. Radiation is often paired with chemotherapy in advanced stages to boost treatment effectiveness.

3. **Chemotherapy**: Chemotherapy drugs are used to kill or stop cancer cells from growing. It can be utilized prior to surgery, for shrinking tumours or after surgery to eliminate remaining cancer cells. **Cisplatin**, **paclitaxel,** and **carboplatin** are commonly used in combination for advanced vulvar cancer.
4. **Targeted Therapy**:

Bevacizumab (Avastin): This drug targets **vascular endothelial growth factor (VEGF)** to avoid the construction of blood vessels that feed the tumour, slowing cancer growth.

EGFR Inhibitors: These block the **epidermal growth factor receptor (EGFR)** in cancers with specific genetic mutations.

5. **Immunotherapy**: **Pembrolizumab** and **nivolumab** are immune checkpoint inhibitors that help the immunity system to recognize and attack cancer cells. These drugs are especially helpful for treating recurrent or metastatic vulvar cancer.
6. **Multidisciplinary Care:** Treating advanced vulvar cancer requires a coordinated effort from a diverse team of medical experts. This team typically includes gynaecologic oncologists, radiation and medical oncologists, plastic surgeons, and specialists in palliative care. By adopting a multidisciplinary approach, the treatment is customized to meet the individual needs of each patient. Beyond managing the cancer itself, this approach focuses on alleviating symptoms, preserving sexual health, and providing emotional and psychological support, ensuring comprehensive care throughout the patient's journey.
7. **Palliative Care:** For patients with metastatic or recurrent vulvar cancer, palliative care plays an essential role in the overall treatment plan. The focus of this care is on managing signs such as pain, ulceration, and bleeding while addressing the emotional and psychological needs of the patient. Palliative care aims to enhance the quality of life by providing comfort and support when curative treatments are no longer viable.
8. **Clinical Trials:** Clinical trials are fundamental to advancing the treatment of vulvar cancer, particularly given its rarity. These trials offer patients the opportunity to access innovative therapies, new drug combinations, or cutting-edge surgical techniques. Involvement in clinical

studies not only provides access to provide effective treatments but also contributes to the ongoing research that enhances the understanding and management of vulvar cancer.

2.5.6 Prevention of Vulvar Cancer

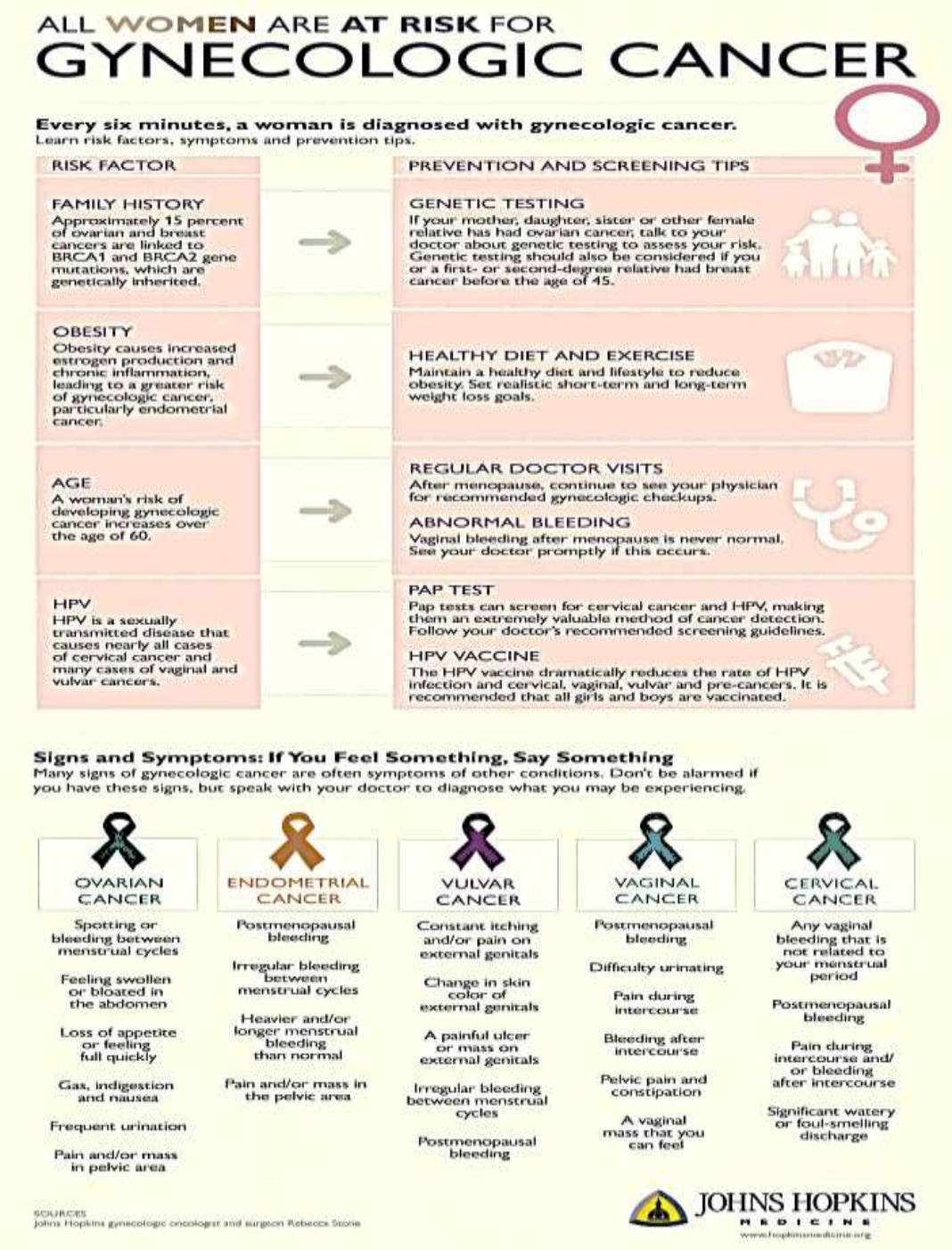
Preventive measures can help lowers the trap of vulvar cancer. These include:

1. **HPV Vaccination**: Getting vaccinated against HPV can significantly reduce the snare of HPV-related cancers, including vulvar cancer.
2. **Safe Sex Practices**: Using condoms and limiting sexual partners reduces the risk of HPV infection.
3. **Quit Smoking**: Avoiding smoking lowers the threat of developing vulvar cancer and many other cancers.
4. **Regular Gynaecological Exams**: Routine pelvic exams can detect precancerous changes or early-stage cancer, allowing for timely treatment.
5. **Monitoring and Treating Pre-Cancerous Conditions**: Conditions like VIN and lichen sclerosis should be monitored and treated promptly to prevent development to cancer.
6. **Self-Examination**: Regular self-examination of the vulva for changes in skin texture, colour, lumps, or sores can help detect abnormalities early.

2.5.7 Early Detection and Follow-Up

Early detection is crucial for successful treatment of vulvar cancer. Regular check-ups, awareness of symptoms, and proactive treatment of pre-cancerous conditions like VIN are key to improving outcomes. When detected early, vulvar cancer is highly treatable, and patients generally have a favourable prognosis. Follow-up care is important to monitor for recurrence or any new developments.

In conclusion, while vulvar cancer is rare, understanding the hazardous factors, recognizing early symptoms, and adopting preventive measures can help reduce the incidence and improve survival rates through early diagnosis and treatment.



3. Conclusion

Gynaecological cancers, which affect the ovaries, cervix, uterus, vulva, and vagina, represent a significant health issue for women around the world. Detecting these cancers early and focusing on prevention are crucial to improving outcomes, as they are often diagnosed at later stages due to their subtle symptoms. Advances in screening techniques, genetic studies, and treatments like targeted therapies and immunotherapy offer hope for better management and improved survival rates. Raising public awareness, encouraging regular screenings, and creating personalized treatment strategies are key to reducing the impact of these cancers and improving women's quality of life. With continued research, there is optimism for the development of more effective approaches for prevention, early detection, and treatment in the future.

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