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Review Article

An Overview of Cervical Cancer and Its Prevention

Rashmi Sumbria*[1], Anjana Thakur[2]

[1]*Department of pharmaceutics, Punjab college of Pharmacy.*
[2]*Department of pharmaceutics, Maharaja Agrasen school of Pharmacy.*

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ABSTRACT

Cervical cancer remains a leading gynecological malignancy and an important global health challenge, particularly in low- and middle-income regions. The disease originates in the cervix when epithelial cells undergo genetic and molecular changes, most often triggered by persistent infection with high-risk human papillomavirus (HPV) strains, mainly HPV-16 and HPV-18. While HPV infection is widespread, additional cofactors—including smoking, high parity, long-term oral contraceptive use, immunosuppression, and lack of screening—contribute to malignant progression. Histologically, squamous cell carcinoma represents the majority of cases, followed by adenocarcinoma, adenosquamous carcinoma, and rarer aggressive variants. Clinical presentation ranges from asymptomatic disease detected through screening to symptoms such as abnormal bleeding, unusual discharge, pelvic pain, and advanced complications involving the urinary or gastrointestinal tract. Diagnostic evaluation integrates screening tools (Pap smear and HPV DNA testing), colposcopy with targeted biopsy, and imaging for staging. Treatment strategies depend on disease stage, ranging from fertility-sparing surgery in early cases to chemoradiotherapy and systemic therapy for advanced or recurrent disease. In recent years, therapeutic advances have significantly expanded options for patients with persistent or metastatic disease. These include immune checkpoint inhibitors, antibody–drug conjugates, precision-targeted therapies guided by molecular profiling, and experimental immunotherapies such as therapeutic HPV vaccines. Integration of these modalities into multidisciplinary care has improved survival and quality-of-life outcomes. This review highlights the epidemiology, pathogenesis, clinical features, diagnostic pathways, and evolving therapeutic landscape of cervical cancer, with emphasis on recent innovations that may contribute to the World Health Organization's goal of eliminating cervical cancer as a public health problem.

INTRODUCTION

***Corresponding Author:** Rashmi Sumbria
Address: *Department of pharmaceutics, Punjab college of Pharmacy.*
Email ✉: rashmisumbria@gmail.com

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Cervical cancer remains a significant gynecological malignancy and a major public health concern, particularly in low- and middle-income countries. It arises in the cervix, the lower part of the uterus that connects to the vagina. The disease develops when cervical epithelial cells undergo genetic alterations, leading to uncontrolled proliferation and invasion of surrounding tissues[1]. The most important causative factor is persistent infection with oncogenic human papillomavirus (HPV) strains, particularly HPV 16 and HPV 18, which are collectively responsible for the majority of cases worldwide[2]. Although HPV infection is common, only a subset of women progress to cancer due to the influence of cofactors such as early sexual activity, multiple pregnancies, long-term use of oral contraceptives, smoking, immunosuppression, and lack of routine screening[3,4]. Cervical cancer is largely preventable through the implementation of HPV vaccination and regular screening. The vaccines currently available are highly effective in reducing the incidence of precancerous lesions and invasive disease[5]. Screening methods, including Pap smears and HPV DNA testing, allow for early identification and treatment of precancerous changes before malignant transformation occurs[4]. Despite these preventive strategies, cervical cancer continues to cause considerable morbidity and mortality worldwide. More than 600,000 new cases and over 340,000 deaths are reported annually, with the highest burden in resource-limited regions[2]. To address this, the World Health Organization (WHO) has developed a global strategy aiming to eliminate cervical cancer as a public health problem through universal vaccination, screening, and timely treatment[2].

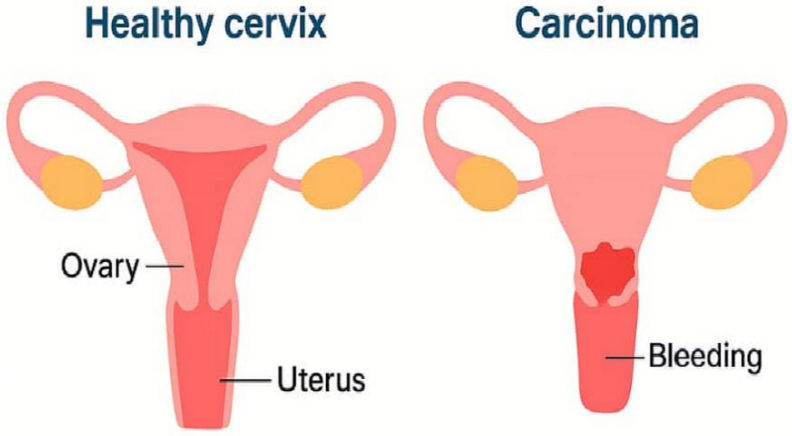

Figure1: Cervical Cancer

Types of Cervical Cancer

Cervical cancer is classified based on the type of epithelial cell from which it originates. The two main histological types are **squamous cell carcinoma** and **adenocarcinoma**, while several rare variants also exist.

1. Squamous Cell Carcinoma (SCC)

- Accounts for approximately **70–80%** of all cervical cancers [6].
- Originates from the **squamous epithelial cells** lining the ectocervix.
- Strongly associated with persistent infection by high-risk HPV, especially **HPV-16**.
- Typically arises in the **transformation zone**, where squamous and glandular cells meet.

2. Adenocarcinoma

- Represents around **10–20%** of cervical cancers[7].
- Originates from the **glandular (columnar) epithelial cells** of the endocervical canal.
- More difficult to detect by Pap smear compared to SCC, because lesions often develop higher in the cervical canal.
- Strongly associated with **HPV-18** infection.

3. Adenosquamous Carcinoma

- A rare form showing features of both squamous cell carcinoma and adenocarcinoma within the same tumor.
- Accounts for about **3–5%** of cases[8].

4. Rare Types

Although uncommon, other histological subtypes include:

- **Small cell neuroendocrine carcinoma** – aggressive, fast-spreading form associated with HPV infection[9].
- **Glass cell carcinoma** – a rare variant of adenosquamous carcinoma with poor prognosis.
- **Sarcomas, lymphomas, and melanomas of the cervix** – extremely rare but possible[9].

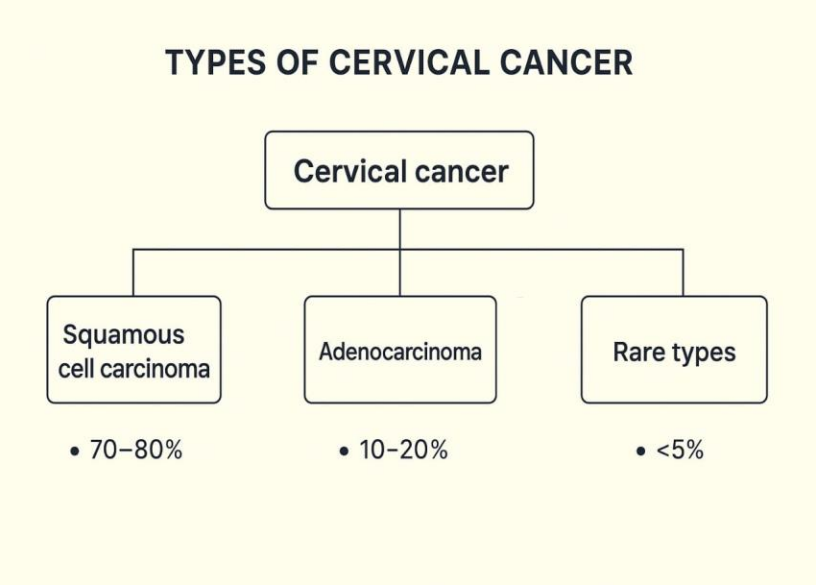

Fig 2- Types of cervical cancer

Causes of Cervical Cancer

Cervical cancer primarily arises from persistent infection with high-risk human papillomavirus (HPV) types, particularly HPV-16 and HPV-18. These oncogenic viruses produce proteins (E6/E7) that disrupt the function of tumor suppressor genes, triggering abnormal cell growth and potentially cancerous progression[10]. However, the presence of HPV alone does not always lead to cancer. A number of cofactors influence the progression from HPV infection to cervical cancer:

- **Smoking** is strongly implicated in elevating risk. Tobacco carcinogens impair local

immune defenses and have been detected in cervical mucus, increasing the likelihood of malignant transformation among HPV-infected women [11,12].

- **Co-infection with other sexually transmitted infections (STIs)**, such as Chlamydia trachomatis, may facilitate persistent HPV infection and promote cervical carcinogenesis[9].
- **High parity (multiple full-term pregnancies)** has been linked with elevated risk, possibly due to hormonal fluctuations and increased susceptibility during pregnancy[13].
- **Low socioeconomic status (SES)** is associated with diminished access to screening and healthcare, delaying detection and treatment and thereby increasing disease risk[14].

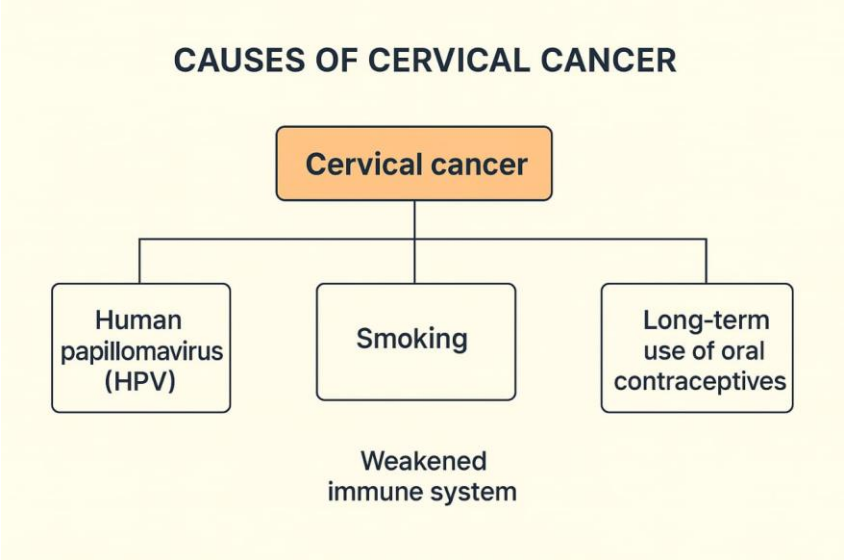

Figure 3- Causes Of Cervical Cancer

Signs and Symptoms of Cervical Cancer

Cervical cancer often develops slowly and may remain asymptomatic in its early stages, which is why regular screening plays a crucial role in detection. When symptoms appear, they may indicate disease progression.

1.**Abnormal Vaginal Bleeding**-The most common presenting symptoms may occur between menstrual periods, after sexual intercourse, or post-menopause [15].

2.**Unusual Vaginal Discharge**-Discharge may be watery, pink, or foul-smelling.Often associated with advanced disease due to necrosis or infection in cervical tissue[16].

3.**PelvicPain**-Persistent pain in the pelvic region or lower back may develop. Pain can radiate to the legs or hips in advanced stages[17].

4. **Pain During Sexual Intercourse (Dyspareunia)**-Caused by tumor growth in the cervix or invasion into surrounding structures[18].

5. **Urinary and Bowel Symptoms**-In later stages, cervical cancer may invade the bladder or rectum, leading to painful urination, hematuria, constipation, or rectal bleeding[19]. The diagnosis of cervical cancer is a stepwise process that begins with screening, followed by confirmatory tests and staging investigations. Early detection is essential for effective treatment and improved survival outcomes.

1. **Screening Methods**

- **Pap smear (cytology):** Identifies abnormal cervical cells that may indicate precancerous lesions or cancer. It remains a cornerstone of early detection strategies[20].

- **HPV DNA testing:** Detects high-risk HPV strains responsible for most cervical cancers, offering higher sensitivity than cytology alone[21].

2. **Colposcopy**

Women with abnormal screening results undergo colposcopy, where the cervix is examined under magnification. Application of acetic acid or Lugol's iodine enhances visualization of abnormal epithelial changes. Suspicious lesions can be targeted for biopsy [22].

3. **Histopathological Examination**

Biopsies—such as punch biopsy, endocervical curettage, or cone biopsy—provide definitive confirmation of invasive cervical cancer. Histology also determines the cancer type (squamous cell carcinoma or adenocarcinoma) and grade[22,23].

4. **Imaging investigations**

Once cancer is confirmed, imaging helps determine local and distant spread. MRI(magnetic resonance imaging) is considered the most accurate for local tumor assessment, while CT (computed tomography)and PET (positron emission tomography scan),CT are used to detect nodal and distant metastases [23,24].

Cure and Treatment of Cervical Cancer

The management of cervical cancer depends on the stage of disease, patient's age, comorbidities, fertility desires, and overall health status. Treatment typically involves a combination of surgery, radiotherapy, chemotherapy, or targeted therapies.

1. Early-Stage Disease

- **Surgery:** For very early stages (IA1 and IA2), procedures such as conization or simple hysterectomy may be sufficient, especially for women wishing to preserve fertility. In stage IB and selected IIA cases, radical hysterectomy with pelvic lymphadenectomy is the standard surgical option[25].

- **Fertility-preserving surgery:**

- **Radical trachelectomy** combined with lymph node assessment is an alternative for women with early-stage disease who wish to retain fertility[26].

2. Locally Advanced Disease

Concurrent Chemoradiotherapy (CCRT):

The gold-standard treatment for stages IIB–IVA involves external beam radiotherapy (EBRT)combined with intracavitary brachytherapy, given concurrently with cisplatin-based chemotherapy[27].

- This approach improves both local control and overall survival compared to radiotherapy alone.

3. Advanced and Recurrent Disease

- **Systemic Chemotherapy:**

- Cisplatin, carboplatin, and paclitaxel-based regimens remain widely used. Combination chemotherapy provides better outcomes than single-agent regimens[28].

- **Targeted and Immunotherapy:**

  - **Bevacizumab (anti-VEGF antibody)**, when added to chemotherapy, has shown improved overall survival in advanced disease.

  - Immune checkpoint inhibitors, such as pembrolizumab (anti-PD-1 antibody), are increasingly used in recurrent or metastatic cervical cancer with PD-L1 expression[29].

Recent advances in treatment of cervical cancer

Despite progress in prevention and screening, treatment options for recurrent, persistent or metastatic cervical cancer have historically been limited. During the past few years several important advances have changed practice and expanded options for patients.

1. Immune checkpoint inhibition in advanced disease- Immune checkpoint inhibitors (ICIs) have become an established option for PD-L1–positive advanced cervical cancer. Randomized data showed that adding pembrolizumab (an anti-PD-1 antibody) to platinum-based chemotherapy (with or without bevacizumab) improved progression-free and overall survival in patients with persistent, recurrent or metastatic disease, establishing chemo-immunotherapy as a new standard in selected patients. ICIs are also being evaluated in earlier lines and in combination with radiation or targeted agents. [30,31]

2. Antibody–drug conjugates (ADCs) — a new drug class with proven survival benefit Tisotumab vedotin (an ADC targeting tissue factor and carrying a cytotoxic payload) has demonstrated clinically meaningful activity in previously treated recurrent/metastatic cervical cancer and gained regulatory approval. Recent randomized data and regulatory decisions have supported its role as an option after progression on prior chemotherapy, representing the first ADC to show an overall-survival benefit in this setting. Ongoing trials are exploring combinations (e.g., ADC + ICI or ADC + chemotherapy) to increase response rates and durability.[32,33]

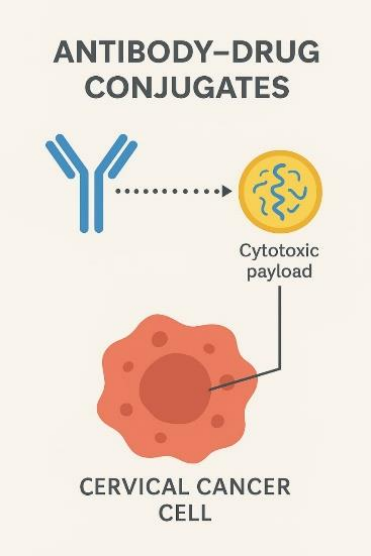

Figure 4

3. Precision/targeted approaches and biomarker-driven therapy- Molecular profiling of cervical tumors is uncovering actionable alterations in small subsets of patients (e.g., DNA damage repair gene alterations). Case reports and early studies suggest that PARP inhibitors and other targeted agents may benefit molecularly selected patients, prompting prospective trials of PARP inhibitors, tyrosine kinase inhibitors and other small molecules in genomically defined cohorts. Wider use of next-generation sequencing is enabling personalized therapy for a minority of patients.[34]

4. Therapeutic vaccines and novel immunotherapies- Therapeutic (non-prophylactic) vaccines directed against HPV oncoproteins (E6/E7) and combination vaccine + ICI strategies are an active area of clinical research. Early-phase trials have shown immune activation and clinical responses in premalignant lesions and some invasive cancers; larger

combination studies are underway to assess whether vaccines can improve outcomes when added to standard therapies. Adoptive T-cell therapies (including engineered T-cell approaches) are also in early clinical testing for HPV-driven cancers.[35]

5. Improvements in multimodality care and guideline updates- Clinical practice guidelines have adapted to incorporate these new systemic options and emphasize multidisciplinary care. Better integration of systemic therapy advances (immunotherapy, ADCs, targeted agents) with contemporary radiation techniques (image-guided brachytherapy) and surgical decision algorithms has refined treatment sequencing and palliation — leading to improved disease control and quality-of-life outcomes for many patients.[31,36]

6. Future directions- Research priorities include rational combinations (e.g., ADC + ICI, vaccine + ICI), identification of predictive biomarkers to select patients most likely to benefit, and expanding access to clinical trials globally. The goal is to convert more durable responses into long-term control while maintaining tolerability.

CONCLUSION

Cervical cancer continues to be a significant global health concern despite being largely preventable through HPV vaccination and effective screening programs. Persistent infection with high-risk HPV types remains the central etiological factor, with additional cofactors contributing to progression from precancerous lesions to invasive disease. Early detection through cytology, HPV testing, and timely diagnostic evaluation is critical for improving survival outcomes. Treatment strategies are stage-specific, ranging from fertility-preserving surgical techniques for early-stage disease to concurrent chemoradiotherapy for locally advanced cases and systemic therapy for metastatic disease. The emergence of immune checkpoint inhibitors, antibody–drug conjugates, targeted therapies, and therapeutic vaccines has revolutionized management, offering hope for improved survival and quality of life even in advanced or recurrent settings. A multidisciplinary approach integrating prevention, early detection, and personalized treatment strategies remains the cornerstone for reducing cervical cancer incidence and mortality worldwide. Continued research and equitable access to vaccination and novel therapies will be key to achieving global cervical cancer elimination goals.

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