



## CERVICAL CANCER: A REVIEW STUDY

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**ABSTRACT** Cervical cancer is a serious health issue originating from the cervix, the lowest part of the uterus, characterized by abnormal rapid cell growth resulting in a tumor. Risk factors include young sexual intercourse, multiple sexual partners, smoking, high parity, and low socio-economic levels. High-risk or oncogenic HPV infections are the primary cause of pre-cancerous and cancerous cervical lesions, with most cases occurring due to HPV16 and 18. Reproductive and sexual factors also increase the risk in people with multiple sexual partners. Oral contraceptive pills are known to be a risk factor for cervical cancer, with the relative risk increasing with the duration of OC use. Cervical cancer is the fourth most common cancer in women worldwide and causes around 350,000 deaths annually. Cervical Squamous Cell Carcinoma (SCC) is the most common type, accounting for 80% to 90% of cases. Adenocarcinoma (AC) constitutes 10% to 20% of all cervical cancers and originates from glandular cells within the cervix. Treatment options include surgery, radiation therapy, chemotherapy, and other medications. Preventative measures include the HPV vaccine, regular screening using Pap Smear and HPV Test, and avoiding smoking and using condoms during sex. Treatment options vary based on the stage of the cancer and individual factors.

**KEYWORDS :** Cervical Cancer, Cervix, HPV, Pap Smear

### INTRODUCTION:

The cervix, the lowest part of the uterus, protrudes into the vagina and opens to about four inches during labor. It contains squamous cells in the vaginal part, which are resistant to abrasion and heal quickly. Deeper, columnar cells come from glands producing mucus. The squamous columnar junction is the area where cancer most commonly arises, as it is the transitional point between squamous and columnar cells.

Cancer is a condition characterized by abnormal rapid growth of cells, resulting in the formation of a mass of tissue called a cancerous growth or tumor. These tumours can be benign or malignant, and are typically removed and do not return. Malignant tumours, on the other hand, can enter and damage nearby tissue and organs, making them a significant threat to life.

Cervical cancer is a disease that originates in the cervix. It is caused by the dilation and full opening of the cervix, which contains squamous cells that protect the outside and glandular cells that produce fluid and mucus during ovulation.

### Etiology:

Cervical cancer is a serious health issue that can be caused by various risk factors, including sexual intercourse at a young age, multiple sexual partners, smoking, high parity, and low socio-economic level.

High-risk or oncogenic HPV infections are the primary cause of pre-cancerous and cancerous cervical lesions, with most cases occurring due to infection with HPV16 and 18. The highest prevalence of HPV occurs at the age of 25 years, which could be related to changes in sexual behaviour.<sup>(1,2)</sup> The major mechanisms through which HPV contributes to carcinogenesis involve the activity of two viral oncoproteins, E6 and E7, which interfere with major tumor suppressor genes, P53 and retinoblastoma.<sup>(3)</sup> These oncoproteins are associated with changes in host DNA and virus DNA methylation, which regulate genetic integrity, cell adhesion, immune response, apoptosis, and cellular control.

Human immunodeficiency virus (HIV) is another risk factor for developing infection from high-risk HPV types. Studies have shown a higher rate of persistent HPV infection with multiple oncogene viruses, more abnormal Papanicolaou (Pap) smears, and higher incidence of CIN and invasive cervix carcinoma among people with HIV. Women infected with HIV are at an increased risk of HPV infection at an early age and are at higher risk.<sup>(4)</sup>

Reproductive and sexual factors have also been linked to cervical cancer. One study found that an increased risk of cervical cancer is observed in people with multiple sexual partners<sup>(5)</sup>, and many studies

suggest that women with multiple sexual partners are at high risk for HPV acquisition and cervical cancer.<sup>(6,7)</sup> The association remained even after controlling for the status of HPV infection, which is a major cause of cervical cancer.<sup>(8)</sup>

Oral contraceptive (OC) pills are known to be a risk factor for cervical cancer. An international collaborative epidemiological study of cervical cancer found that the relative risk in current users increased with an increase in the duration of OC use.<sup>(9)</sup> A multi-center case-control study found that the risk of cervical cancer increased by 3 times if women tested positive for HPV DNA.<sup>(10)</sup> A recent systematic review & meta-analysis suggested that OC pill use had a definite associated risk for developing cervical cancer, especially for adenocarcinoma.<sup>(11)</sup>

### Epidemiology:

Cervical cancer is a significant global health issue, with the fourth most common cancer in women worldwide and around 350,000 deaths annually.<sup>(12,13)</sup> The highest rates of cervical cancer incidence and mortality are observed in low- and middle-income countries.<sup>(13)</sup> The primary cause of cervical cancer is human papillomavirus (HPV) infection, which can lead to the development of abnormal cells that may progress to cancer over time. Women living with HIV are six times more likely to develop cervical cancer.<sup>(13)</sup>

Cervical cancer is a significant health concern in Asia, ranking as the fourth most common cancer among women globally and the fourth leading cause of cancer-related deaths.<sup>(14)</sup> Survival rates for cervical cancer in Asian countries vary across different time periods, with the highest rates in Eastern Africa (including Zimbabwe) and relatively lower rates in Western Asia. In Southeast Asia, cervical cancer is the second most common cancer in women and a major cause of cancer-related deaths in low- and middle-income countries (LMICs) like Nepal.<sup>(15)</sup>

Cervical cancer is a significant health concern in India, ranking as the second most common cancer among women. Despite decreasing incidence rates, it still accounts for 10% of all female cancers in the country.<sup>(16)</sup> The overall 5-year relative survival for all cervical cancers in India is approximately 46%, with survival rates varying significantly based on the stage at diagnosis.<sup>(17)</sup> The peak age for cervical cancer incidence in India is 55-59 years, with regional variation, with some areas reporting higher levels of cervical cancer.<sup>(18)</sup> The 5-year observed survival (ASRS) for cervical cancer in India is approximately 51.7%, with notable variations across different cities.<sup>(16)</sup> Infections with HPV types 16 and 18 are responsible for four out of every five cervical cancers reported in India.<sup>(16)</sup>

### Pathophysiology:

Cervical cancer develops slowly over years, with cells in the cervix undergoing various changes before turning into cancerous cells. The

main cause is the human papillomavirus (HPV), transmitted through sexual contact.<sup>(19)</sup> The immune system typically clears the virus, but in some cases, it persists for years, leading to changes in cervical cells. The altered cells multiply rapidly, defying the natural cell life cycle, resulting in an excess of cells that can form a tumor.<sup>(20)</sup> Cancerous cells can invade and destroy healthy tissues in the cervix, potentially breaking away from the primary tumor and spreading to other parts of the body.

### Histopathology:

Cervical Squamous Cell Carcinoma (SCC) is the most common type of cervical cancer, accounting for 80% to 90% of cases.<sup>(21)</sup> It arises from neoplastic cells with varying degrees of squamous differentiation and is associated with high-risk human papillomavirus (HPV). HPV types 16 and 18 are predominantly linked to SCC, with SCC morphology varying and several histologic variants described.<sup>(21)</sup> Adenocarcinoma (AC) constitutes 10% to 20% of all cervical cancers and originates from glandular cells within the cervix. AC is less commonly associated with HPV and is a rare subtype composed of mixed glandular and squamous elements.<sup>(22)</sup> Cervical cancer is the fourth most common cancer worldwide among women, causing significant mortality. Incidence varies based on screening practices, with a ~75% decrease in countries with screening programs over the past 50 years. Most patients with cervical cancer are between 40 and 54 years old.<sup>(21)</sup>

### Histology of CIN

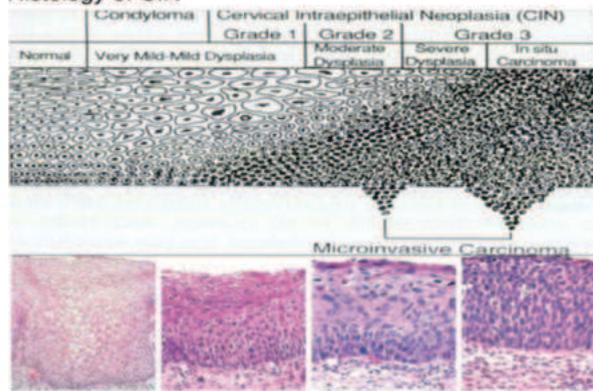


Figure 1: Histology of Cervical Cancer

### Differential Diagnosis:

Cervical cancer is a rare condition that can cause abnormal vaginal bleeding. Differential diagnoses include cervical polyp, cervical leiomyoma (fibroid), invasion from primary uterine malignancy, vaginal cancer, cervical lymphoma, metastases to the cervix, and cervical ectopic pregnancy.

Cervical polyp is a benign growth on the cervix that can cause bleeding. Cervical leiomyoma is a non-cancerous tumor arising from the smooth muscle of the cervix. Invasion from primary uterine malignancy is a cervical involvement due to uterine cancer. Vaginal cancer is rare but can present with similar symptoms.

### Diagnosis:

Cervical cancer diagnosis involves various tests, including the Pap Test (Pap Smear), HPV DNA Test, Colposcopy, Biopsy Techniques, and Staging Tests.

The Pap Test is a common screening test that involves collecting cells from the cervix and examining them for abnormalities. The HPV DNA Test checks for infection with high-risk human papillomavirus (HPV) types associated with cervical cancer.<sup>(23)</sup>

Diagnostic procedures include Colposcopy, which uses a special magnifying instrument to examine the cervix for signs of cancer, and Biopsy Techniques, such as Punch Biopsy, Endocervical Curettage, Electrical Wire Loop (LEEP), and Cone Biopsy (Conization).<sup>(23)</sup>

Staging Tests determine the extent of the cancer, using imaging tests like X-rays, MRI, CT scans, and PET scans. Visual Examination may also be performed to evaluate cancer spread.<sup>(24)</sup>

### Treatment/Management:

Cervical cancer treatment options vary based on the stage of the cancer and individual factors. Common treatments include surgery, radiation

therapy, chemotherapy, and other medications. Surgery involves removing the cervix and uterus along with the cancerous tumor, while radiation therapy uses high-powered energy beams to target and kill cancer cells. Chemotherapy involves injected medications into a vein to kill cancer cells, sometimes used alongside radiation therapy. Other medications include Bevacizumab, Carboplatin, Cisplatin, Docetaxel, Fluorouracil (5-FU), and Gemcitabine. Diagnostic procedures include Pap smear, HPV DNA Test, cone biopsy, punch biopsy, and endocervical curettage.

**Prevention:** To prevent cervical cancer, follow these precautions:

- HPV vaccine, which protects against the most common types of HPV that cause cervical, vaginal, and vulvar cancers. It is recommended for preteens aged 11 to 12 years, but can be given starting at age 9. Adults up to age 26 who haven't been vaccinated can also consider getting the HPV vaccine.<sup>(25)</sup>
- Regularly screen for cervical cancer, using two screening tests: Pap Test (Pap Smear) and HPV Test.<sup>(25)</sup>
- Avoid smoking and use condoms during sex, although condom effectiveness in preventing HPV is uncertain but precautions should be taken to prevent from Cervical Cancer.<sup>(25)</sup>

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