



Review Article

Cervical Cancer – A Review

Jadon Gunjan*, Bhadauria R. S., Diwaker A. K.¹, Joshi K. S.

*Shrinathji Institute of Pharmacy, Nathdwara, Rajsamand (Raj.) India 313301

¹Nitin Life Sciences, Himachal, India

Cancer refers to a class of diseases in which a cell or a group of cells divide and replicate uncontrollably, intrude into adjacent cells and tissues (invasion) and ultimately spread to other parts of the body than the location at which they arose (metastasis) (National Cancer Institute 2009). Cervical Cancer is malignant Carcinoma type of cancer originate in cervix region. The cervix is the narrow portion of the uterus where it joins with the top of the vagina. Most cervical cancers are squamous cell carcinomas, arising in the squamous (flattened) epithelial cells that line the cervix. Adenocarcinoma, arising in glandular epithelial cells is the second most common type. Very rarely, cancer can arise in other types of cells in the cervix. In cervical cancer, (cancer of the *uterine cervix*), cancer develops in the tissues of the cervix, which is a part of the female reproductive system. The cervix connects the upper body of the uterus to the vagina. The *endocervix* (the upper part which is close to the uterus) is covered by glandular cells, and the *ectocervix* (the lower part which is close to the vagina) is covered by squamous cells. The *transformation zone* refers to the place where these two regions of the cervix meet (American Cancer Society 2009).

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INTRODUCTION

Cervical cancer is the term for a malignant neoplasm arising from cells originating in the cervix uteri. One of the most common symptoms of cervical cancer is abnormal vaginal bleeding, but in some cases there may be no obvious symptoms until the cancer has progressed to an advanced stage. Human papillomavirus (HPV) infection appears to be a necessary factor in the development of almost all cases

(90+ %) of cervical cancer. Histologic subtypes of invasive cervical carcinoma include the following. Though squamous cell carcinoma is the cervical cancer with the most incidences, the incidence of adenocarcinoma of the cervix has been increasing in recent decades¹.

Types of Cervical Cancer :

- squamous cell carcinoma (about 80-85%)
- adenocarcinoma (about 15% of cervical cancers in the UK)
- adenosquamous carcinoma

*Address for correspondence

jadon_gunjan@yahoo.in

- small cell carcinoma
- neuroendocrine tumour
- glassy cell carcinoma
- villoglandular adenocarcinoma
- Melanoma (Non Carcinoma Maligancies of Cervix)
- Lympho (Non Carcinoma Maligancies of Cervix)¹.

Causes, incidences, and risk factors (etiology):

Worldwide, cervical cancer is the third most common type of cancer in women. It is much less common in the United States because of the routine use of Pap smears.

Cervical cancers start in the cells on the surface of the cervix. There are two types of cells on the cervix's surface: squamous and columnar. Most cervical cancers are from squamous cells.

Cervical cancer usually develops very slowly. It starts as a precancerous condition called dysplasia. This precancerous condition can be detected by a Pap smear and is 100% treatable. It can take years for precancerous changes to turn into cervical cancer. Most women who are diagnosed with cervical cancer today have not had regular Pap smears or they have not followed up on abnormal Pap smear results.

Almost all cervical cancers are caused by HPV (human papilloma virus). HPV is a common virus that is spread through

sexual intercourse. There are many different types of HPV. Some strains lead to cervical cancer. (Other strains may cause genital warts, while others do not cause any problems at all.)

A woman's sexual habits and patterns can increase her risk for cervical cancer. Risky sexual practices include having sex at an early age, having multiple sexual partners, and having multiple partners or partners who participate in high-risk sexual activities.

Risk factors for cervical cancer include²:

- Not getting the HPV vaccine
- Poor economic status
- Women whose mothers took the drug DES (diethylstilbestrol) during pregnancy in the early 1960s to prevent miscarriage
- Weakened immune system

Symptoms:

Most of the time, early cervical cancer has no symptoms. Symptoms that may occur can include:

- Abnormal vaginal bleeding between periods, after intercourse, or after menopause
- Continuous vaginal discharge, which may be pale, watery, pink, brown, bloody, or foul-smelling
- Periods become heavier and last longer than usual.

Cervical cancer may spread to the bladder,

intestines, lungs, and liver. Patients with cervical cancer do not usually have problems until the cancer is advanced and has spread. Symptoms of advanced cervical cancer may include²:

- Back pain
- Bone pain or fractures
- Fatigue
- Leaking of urine or feces from the vagina
- Leg pain
- Loss of appetite
- Pelvic pain
- Single swollen leg
- Weight loss

Signs and Tests:

Precancerous changes of the cervix and cervical cancer cannot be seen with the naked eye. Special tests and tools are needed to spot such conditions^{2,3}.

- Pap smears screen for precancers and cancer, but do not make a final diagnosis.
- If abnormal changes are found, the cervix is usually examined under magnification. This is called colposcopy. Pieces of tissue are surgically removed (biopsied) during this procedure and sent to a laboratory for examination.
- Cone biopsy may also be done.

If the woman is diagnosed with cervical cancer, the health care provider will order

more tests to determine how far the cancer has spread. This is called staging. Tests may include³:

- Chest x-ray
- CT scan of the pelvis
- Cystoscopy
- Intravenous pyelogram (IVP)
- MRI of the pelvis

Treatment:

Treatment of cervical cancer depends on⁴:

- The stage of the cancer
- The size and shape of the tumor
- The woman's age and general health
- Her desire to have children in the future

Early cervical cancer can be cured by removing or destroying the precancerous or cancerous tissue. There are various surgical ways to do this without removing the uterus or damaging the cervix, so that a woman can still have children in the future.

Surgical Therapy:

- **Loop electrosurgical excision procedure (LEEP)** -- uses electricity to remove abnormal tissue
- **Cryotherapy** -- freezes abnormal cells
- **Laser therapy** -- uses light to burn abnormal tissue

A hysterectomy (removal of the uterus but not the ovaries) is not often performed for cervical cancer that has not spread. It may

be done in women who have repeated LEEP procedures.

Treatment for more advanced cervical cancer may include:

- **Radical hysterectomy**, which removes the uterus and much of the surrounding tissues, including lymph nodes and the upper part of the vagina. Surgical removal of the uterus, cervix, and part of the vagina. In some cases, the ovaries, fallopian tubes, and lymph nodes are removed. A radical hysterectomy may be combine with chemotherapy or radiation therapy.
- **Pelvic exenteration**, an extreme type of surgery in which all of the organs of the pelvis, including the bladder and rectum, are removed.
- **Lymphadenectomy**, Surgical removal of the lymph nodes. It is common in treating women with cervical cancer.
- **Radical Trachelectomy** Removal of the cervix and its surrounding tissue while leaving the body of the uterus intact. A radical trachelectomy with lymphadenectomy is an option for young women with early stage disease who wish to maintain fertility.

Radiation Therapy:

Radiation may be used to treat cancer that has spread beyond the pelvis, or cancer that has returned. Radiation therapy is either external or internal.

- **Internal radiation therapy** uses a device filled with radioactive material, which is placed inside the woman's vagina next to the cervical cancer. The device is removed when she goes home.
- **External radiation therapy** beams radiation from a large machine onto the body where the cancer is located. It is similar to an x-ray.

Chemotherapy :

Chemotherapy uses drugs to kill cancer. Some of the drugs used for cervical cancer chemotherapy include 5-FU, cisplatin, carboplatin, ifosfamide, paclitaxel, and cyclophosphamide. Sometimes radiation and chemotherapy are used before or after surgery.

Expectations (Prognosis) :

How well the patient does depends on many things, including^{3,4}:

- The type of cancer
- The stage of the disease
- The woman's age and general physical condition
- If the cancer comes back after treatment

Pre-cancerous conditions are completely curable when followed up and treated properly. The chance of being alive in 5 years (5-year survival rate) for cancer that has spread to the inside of the cervix walls but not outside the cervix area is 92%.

The 5-year survival rate falls steadily as the cancer spreads into other areas.

Complications:

- Some types of cervical cancer do not respond well to treatment.
- The cancer may come back (recur) after treatment.
- Women who have treatment to save the uterus have a high risk of the cancer coming back (recurrence).
- Surgery and radiation can cause problems with sexual, bowel, and bladder function.

Calling Your Health Provider:

Call your health care provider if you:

- Have not had regular Pap smears
- Have abnormal vaginal bleeding or discharge

Prevention:

A vaccine to prevent cervical cancer is now available. In June 2006, the U.S. Food and Drug Administration approved the vaccine called Gardasil, which prevents infection against the two types of HPV responsible for most cervical cancer cases. Studies have shown that the vaccine appears to prevent early-stage cervical cancer and precancerous lesions. Gardasil is the first approved vaccine targeted specifically to prevent any type of cancer. Practicing safe sex (using condoms) also reduces your risk of HPV and other sexually transmitted diseases. HPV

infection causes genital warts. These may be barely visible or several inches wide. If a woman sees warts on her partner's genitals, she should avoid intercourse with that person.

To further reduce the risk of cervical cancer, women should limit their number of sexual partners and avoid partners who participate in high-risk sexual activities.

Getting regular Pap smears can help detect precancerous changes, which can be treated before they turn into cervical cancer. Pap smears effectively spot such changes, but they must be done regularly. Annual pelvic examinations, including a pap smear, should start when a woman becomes sexually active, or by the age of 20 in a nonsexually active woman³.

If you smoke, quit. Cigarette smoking is associated with an increased risk of cervical cancer².

Vaccine For Cervical Cancer:

Two vaccines, Gardasil and Cervarix, are available to prevent HPV infection.

Gardasil (Merck & Co.), also known as Gardasil or Silgard^{5,6}, is a vaccine for use in the prevention of certain types of human papillomavirus (HPV),⁷ specifically HPV types 6, 11, 16 and 18.^{8,9} HPV types 16 and 18 cause an estimated 70% of cervical cancers,^{10,11} and are responsible for most HPV-induced anal,¹² vulvar, vaginal,¹³ and penile cancer cases. HPV types 6 and 11

cause an estimated 90% of genital warts cases.

Gardasil has been used in prevention of two types of HPV infections, associated with approximately 70% of HPV cases. It does not treat existing infection. Therefore, to be effective it must be given before HPV infection occurs. The HPV strains that Gardasil protects against are sexually transmitted. It was approved in the US on June 8, 2006 by the U.S. Food and Drug Administration (FDA). The FDA recommends vaccination before adolescence and potential sexual activity^{8,14,15}.

Cervarix is a vaccine against certain types of cancer-causing human papillomavirus (HPV).

Cervarix is designed to prevent infection from HPV types 16 and 18, that cause about 70% of cervical cancer cases.¹⁶ These types also cause most HPV-induced genital and head and neck cancers. Additionally, some cross-reactive protection against virus strains 45 and 31 were shown in clinical trials.¹⁷ Cervarix also contains AS04, a proprietary adjuvant that has been found to boost the immune system response for a longer period of time.¹⁸ Cervarix is manufactured by GlaxoSmithKline.

Support Group: National Cervical Cancer Coalition - <http://www.nccc-online.org/>

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