



A Review on: Cervical Cancer

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ABSTRACT

A major global public health issue, cervical cancer mostly affects the cervix and is one of the main causes of illness and death for women globally. The primary cause is the Human Papillomavirus (HPV), which is spread through sexual contact. High-risk strains, such as HPV 16 and 18, account for about 70% of cases. Adenocarcinoma (10–20%) and squamous cell carcinoma (80–90%) are two histological forms in which the illness presents. Due to a lack of awareness, poor screening, and restricted access to preventive treatments, cervical cancer is the second most common cause of cancer-related fatalities in India. In areas like Gujarat, where screening rates are still low and late-stage diagnoses are common, epidemiological data emphasize the impact. Early sexual activity, several pregnancies, smoking, and weakened immunity are risk factors. Pap smears and HPV tests are used for diagnosis, and chemotherapy, immunotherapy, radiation therapy, and surgery are among the available treatment choices. Despite progress, implementation and awareness issues still exist. In order to lower the incidence of cervical cancer and enhance outcomes, especially for marginalized communities, this study emphasizes the significance of HPV vaccination, routine screening, and public health campaigns.

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INTRODUCTION: (1,2,3,4,5,6,7,8,9)



Cervical cancer, a type of cancer that affects the cervix, or lower part of the uterus, is a significant global public health concern. It is a major source of illness and mortality among women globally. Cervical cancer is mostly caused by the Human Papilloma Virus (HPV), which spreads through sexual contact. (1)

The human papillomavirus (HPV), which mainly affects young adults among the ages of 22 and 25, has more than 150 different forms at this time. A class of viruses known as HPV commonly infects young adults who are sexually active in their reproductive systems. Thirteen of the more than 150 HPV strains that have been identified—HPV 16, 18, 35, 31, 39, 45, 51, 52, 56, 58, 59, and 68—are classified as "high risk HPV" (HR-HPV) due to their relatively high carcinogenic potential, which means that they can cause cervical cancer. (2)

HPV types 16 and 18 are responsible for about 70% of all cervical cancer cases globally. The risk of anogenital cancers, such as cervical cancer, may be reduced by human papillomavirus vaccines that protect against HPV 16 and 18. (3)

Cervical cancer, a preventable and treatable disease, continues to be a significant public health concern in India due to its high incidence and mortality rates. Young women in rural areas are disproportionately affected because of low awareness, inadequate screening, and limited access to preventive measures. Cervical cancer is the second most common cause of cancer-related deaths among Indian women. (6)

Human papillomavirus (HPV) vaccination and screening can significantly reduce the incidence of cervical cancer; however, effective implementation requires knowledge of the target population's knowledge, attitude, and practices. (7)

HPV is the most common sexually transmitted infection in the world. Of the more than 200 strains of HPV, most do not cause any symptoms. However, high-risk HPV strains can result in chronic infections and precancerous growths. (8)

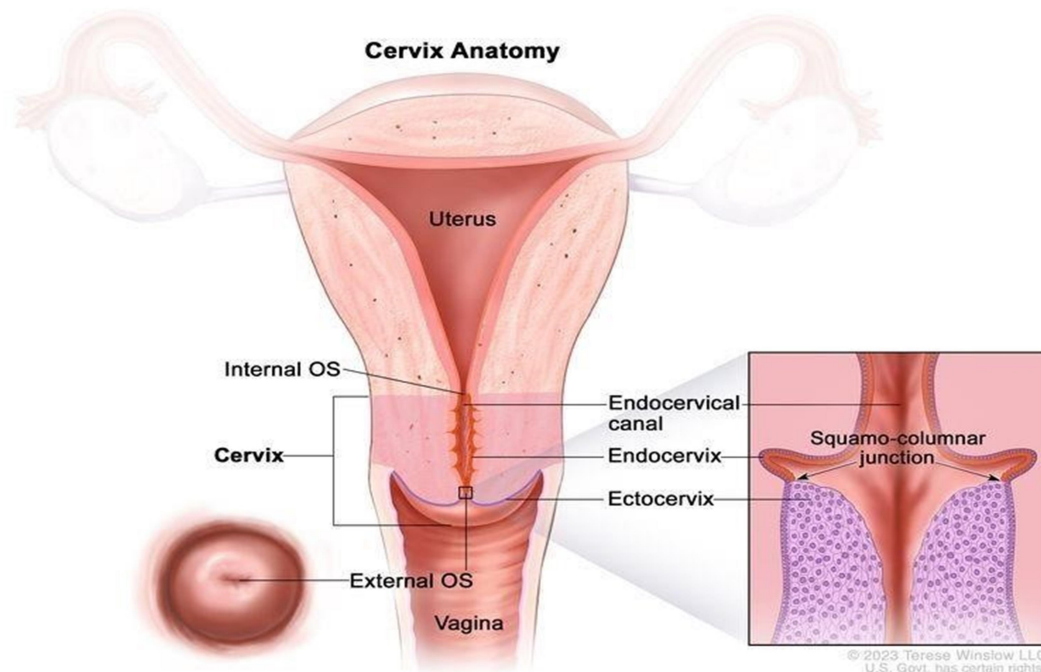


Fig.1 Cervical Cancer Anatomy ⁽⁹⁾

EPIDEMIOLOGY ^(10,11,12,)

- One-fifth of the world's cervical cancer cases are in Gujarat, one of the states affected. The disease claims the lives of about 80,000 Indian women annually, one every seven minutes. ⁽¹⁰⁾
- The chances of survival are significantly reduced because 80% of cervical cancer cases have been identified at stage 3. Among Indian women, cervical cancer is the second most common type of cancer. simply 1.9% of women in Gujarat who are between the ages of 30 and 49 have undergone screening for cervical cancer. ⁽¹⁰⁾
 - Difficulties in Fighting Cervical Cancer: ⁽¹¹⁾
 - Lack of Awareness: A lack of knowledge about cervical cancer and its prevention techniques leads to the high death rate from the disease.
 - Inadequate Screening: A lack of screening programs and training for healthcare professionals prevents early detection.
- • Nonprofit organisations dedicated to early detection and awareness-raising, like the Foundation; • The Gujarat Cancer Research Institute (GCRI) provides patients from Gujarat, Rajasthan, and Madhya Pradesh with subsidised treatment as part of its efforts to combat cervical cancer; • The Indian

government launched cervical cancer screening programs, but there are still issues with their implementation.

- As part of its efforts to fight cervical cancer, the Gujarat Cancer Research Institute (GCRI) offers patients from Madhya Pradesh, Rajasthan, and Gujarat with subsidised treatment.
 - Nonprofit organisations like the Foundation that promote awareness-raising and early detection.
 - Despite the fact that cervical cancer screening programs have been initiated by the Indian government, there are still problems with their execution.
- The Gujarat Cancer Research Institute (GCRI) provide subsidised treatment to patients from Madhya Pradesh, Rajasthan, and Gujarat in an effort to combat cervical cancer. The Indian government has started cervical cancer screening programs, but there are still issues with how they are being conducted out. • The Foundation and other nonprofit organisations that support early detection and awareness-raising. ^(11,12)

ETIOLOGY: ^(12,13,14,)

- The causes of cervical cancer is complex and multifaceted. However, the primary cause is: The human papillomavirus (HPV) is one STD that can lead to cervical cancer.
- 70–80% of cervical cancers are caused by high-risk HPV types (16, 18, 33, 35, 31, 39, 45, 51, 52, 58, 56, 59, 66, and 68). ⁽¹²⁾

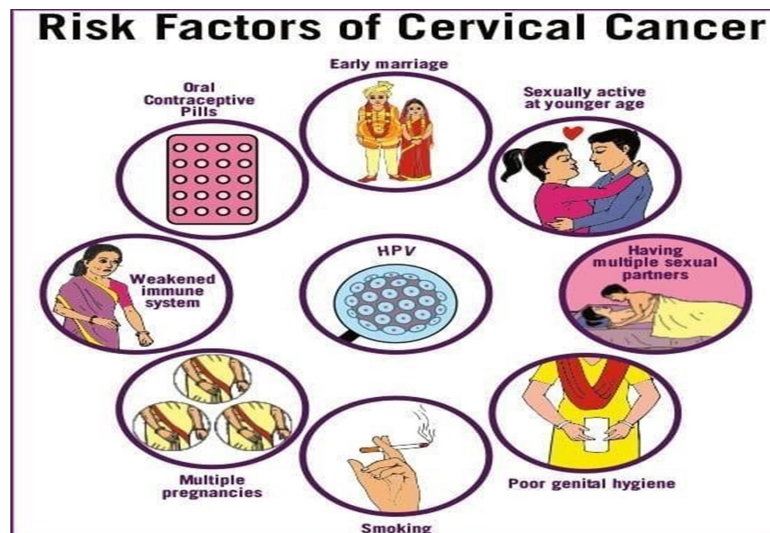


Fig 2. Risk factors of cervical cancer ⁽¹²⁾

Additional variables that raise the risk of cervical cancer include: ^(13,14)



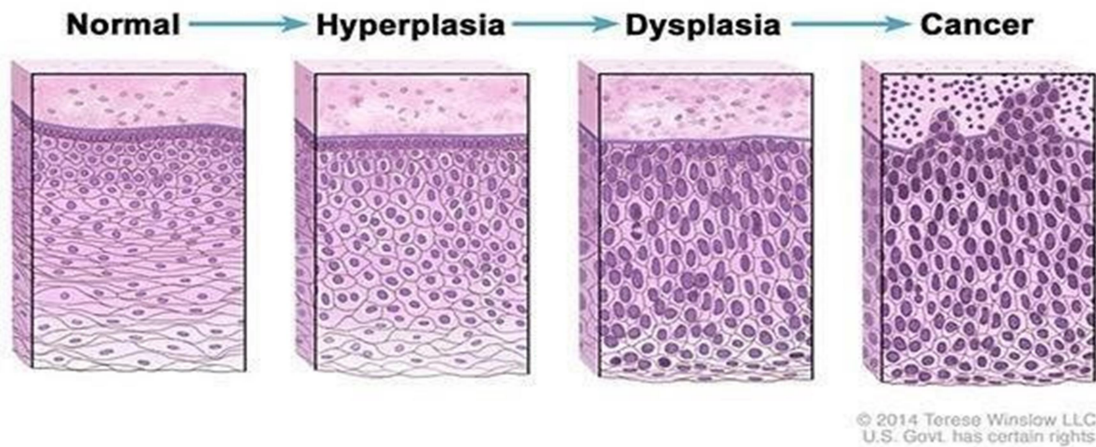
1. Early sexual activity may result from an early marriage. raise the chance of developing cervical cancer.
2. Early sexual debut age: Increases HPV exposure.
3. Having several sexual partners raises the risk of HPV exposure.
4. Inadequate genital hygiene can increase the risk of infection, which can develop into a chronic condition and cause cervical cancer.
5. Multiple pregnancies: A greater number of kids a woman has, the higher her chance for developing cervical cancer.
6. Weakness of the immune system: Lowers the immune system's ability to face HPV infection.
7. Using oral contraceptives for a long time may increase your risk.
8. Smoking: Increases the chance of cervical cancer.
9. Family history: If a first-degree relative has cervical cancer, the risk is elevated.
10. Socioeconomic factors: Lack of education, poor access to healthcare, and a lower socioeconomic status all raise risk.
11. Increased threat of cervical cancer with hormone replacement therapy HPV exposure is increased when other STIs are present.
12. A history of pelvic inflammation may increase the risk of infection, which may worsen over time and leads to cervical cancer.



PATHOPHYSIOLOGY (15,16,17,18,19,20)

Hyperplasia and dysplasia, abnormal cell modifications in the cervix that take place before a normal cell becomes cancerous are actually the cause about cervical cancer. ⁽¹⁵⁾

- ✦ **HYPERPLASIA:** An increase in a tissue or organ's cell count that does not affect the cells' ability to appear normal under a microscope. This may be a reaction to hormone changes, inflammation, or injury. ⁽¹⁶⁾
- ✦ Under a microscope, cells in **DYSPLASIA** appear abnormal, but they are not yet cancerous. As a precancerous condition, dysplasia has the potential to progress to cancer if treatment fails to received. ⁽¹⁶⁾



1. Cervical Intraepithelial Neoplasia (CIN): Precancerous cells that can progress to cancer if left untreated.⁽¹⁷⁾

❖ CIN I: Mild dysplasia (abnormal cell growth)

- While the outer layer of cervix cells are unusual, they are not yet dangerous.
- Only the epithelium, the outermost layer of the cervix, contains the aberrant cells.
- The cells might seem a little enlarged or asymmetrical.

❖ CIN II: Moderate dysplasia

- The abnormal cells are more pronounced and occupy about 1/3 to 2/3 of the thickness of the cervical epithelium.
- The cells may appear more irregularly shaped, with more variability in size and staining.
- The nuclei of the cells may be more abnormal, with more prominent nucleoli.

CIN III: Severe dysplasia (cancerous cells confined to the epithelium)

- The abnormal cells occupy more than 2/3 of the thickness of the cervical epithelium.
- The cells are highly abnormal, with irregular shapes, sizes, and staining.
- The nuclei of the cells are very abnormal, with prominent nucleoli.

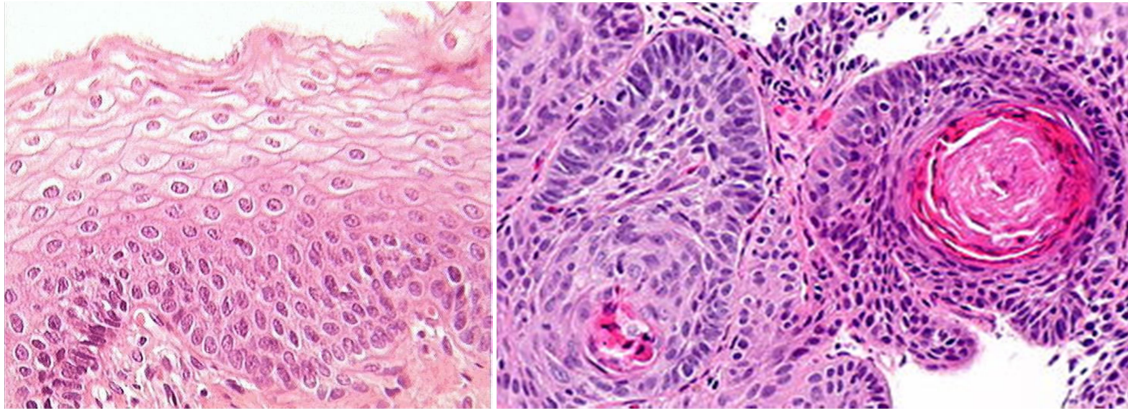
2. Microinvasive carcinoma: Cancer cells invade the stroma (connective tissue) but are still confined to the cervix.⁽¹⁷⁾

3. Invasive carcinoma: Cancer cells invade deeper into the cervix and potentially spread to other tissues.⁽¹⁷⁾

Histological types:⁽¹⁸⁾

- 80–90% of cases are somewhat squamous cell carcinoma, and
- 10–20% are adenocarcinomas.
- Rare cases of adenosquamous carcinoma

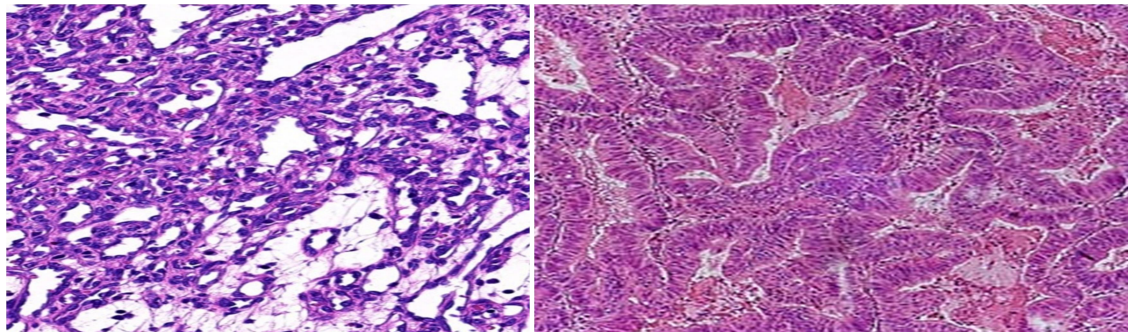
(1) Squamous Cell Carcinoma



(A) Normal Squamous Cell ⁽¹⁸⁾

(B) Squamous Cell Carcinoma ⁽¹⁹⁾

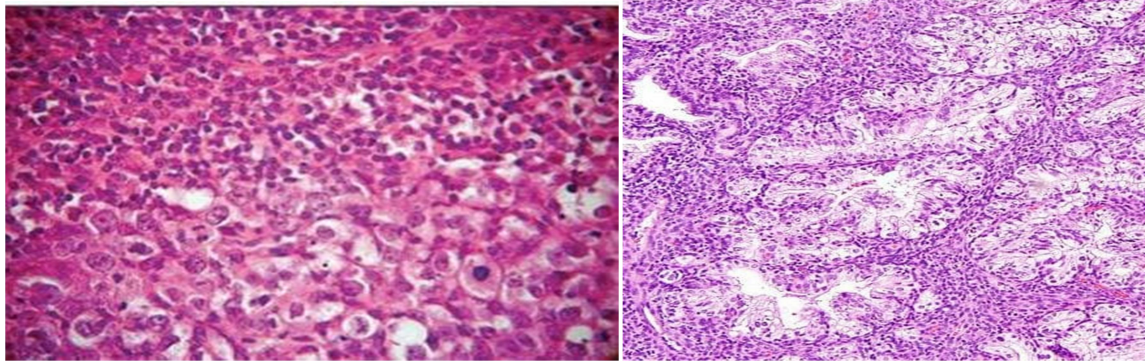
(2) Adeno Cell Carcinoma



(A) Normal Adeno Cell ⁽¹⁸⁾

(B) Adeno Cell Carcinoma ⁽¹⁹⁾

(3) Adenosquamous Cell Carcinoma



(A) Normal Adenosquamous Cell ⁽¹⁸⁾

(B) Adenosquamous cell Carcinoma ⁽¹⁹⁾

Fig.4 Microscopy of histological types

5. Tumour grading: Based on cell differentiation and growth pattern. ⁽²⁰⁾

(A) Well-differentiated (Grade 1)

- Cancer cells resemble normal cells
- Tumour growth is slow
- Prognosis is generally good

(B) Moderately differentiated (Grade 2)

- Cancer cells are slightly abnormal
- Tumour growth is moderate
- Prognosis is fair

(C) Poorly differentiated (Grade 3)

- Cancer cells are highly abnormal
- Tumour growth is rapid
- Prognosis is generally poor

(D) Undifferentiated (Grade 4)

- Cancer cells are extremely abnormal
- Tumour growth is very aggressive
- Prognosis is poor

6. Staging: Based on tumour extent and spread.

- Confined to the cervix in Stage I;

- expanding over the cervix but not to the pelvic wall in Stage II
- Stage III: Spreads to the lower vagina or pelvic wall;
- Stage IV: Spreads to other organs

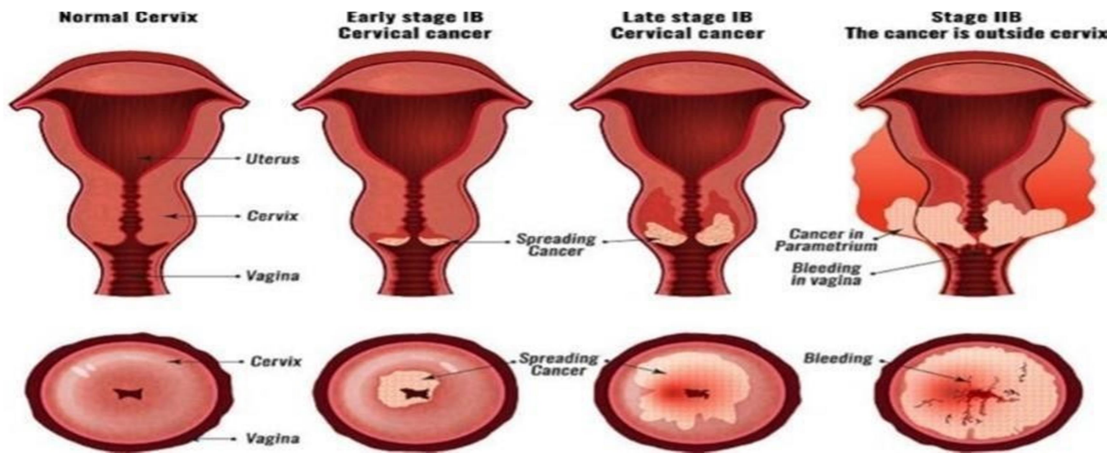


Figure 5: Cervical cancer stages ⁽²⁰⁾

SEVERAL STEPS ARE INVOLVED IN THE DIAGNOSIS OF CERVICAL CANCER. ^{:(21,22,23)}

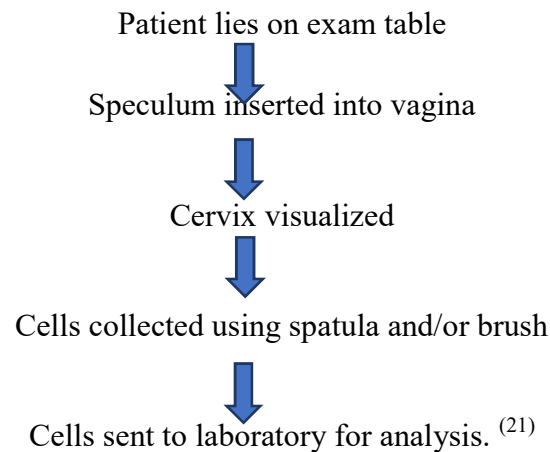
Screening Tests:

1. Pap Smear (Pap Test): Examines cervical cells for abnormalities.

- A medical procedure called a Pap smear, also known as a Pap test, involves taking cells from the cervix in order to identify abnormal cell changes, such as cancer and precancerous conditions. Every three years, women between the ages of 21 and 29 who have a cervix should get a Pap smear alone.— Every five years, high-risk HPV testing and a Pap smear are recommended for women with a cervix who are between the ages of thirty and sixty-five. ⁽²¹⁾
- The primary purposes of a Pap smear test are threefold. ⁽²²⁾
 1. Early detection of cervical cancer
 2. Identification of precancerous cells
 3. Monitoring of cervical health



Procedure: ⁽²¹⁾



Types of Pap Smears: ⁽²²⁾

1. The traditional Pap smear
2. LBC, and liquid-based cytology
3. The Pap test via thin prep

1. Conventional Pap Smear

- Cells extracted from the cervix with a brush or spatula
- Smear placed on glass slide
- Examined under microscope

2. Liquid-Based Cytology (LBC)

- Cells harvested from the cervix via a scalpel or the spatula
- Cells suspended in liquid medium
- Automated analysis

3. Thin Prep Pap Test.

- Cells extracted from the cervix alongside an instrument or spatula
- Cells suspended in preservative solution
- Filtered and analysed.



High-risk HPV types are identified by the Human Papillomavirus (HPV) test. ⁽²³⁾

Cervical cancer and other health problems can be caused by the common sexually transmitted virus known as the human papillomavirus (HPV).

Cervical cells containing high-risk HPV types that have the potential to develop into cancer are detected by the HPV test.

▪ **Types of HPV tests:**

1. HPV DNA Tests: These tests identify the virus's genetic material, or DNA. Cervical associated with cancer high-risk HPV types can be detected by these tests.
2. HPV RNA Tests: These tests identify the virus's genetic material, or RNA. Cervical linked to cancer high-risk HPV types can be detected by these tests.
3. The third test is the Pap test with HPV Reflex, which combines the two tests.
4. The HPV test is carried out to find out whether HPV is present if the Pap test is abnormal. The HPV genotyping test affects the particular HPV type that is present in the cells.
5. HPV mRNA test: This test finds the HPV virus's messenger RNA (mRNA) in cells.

✚ **CERVICAL CANCER SYMPTOMS AND VARIABLES** ^(24,25)

- It is difficult to identify women with early cervical cancers and pre-cancer because they typically don't have any symptoms. Usually, symptoms appear after the cancer has spread. ⁽²⁴⁾
- When early-stage cervical cancer symptoms do appear, they could include ⁽²⁴⁾
- Post-sex vaginal bleeding.
- After menopause,
- vaginal bleeding occurs.
- Vaginal bleeding during or after heavier or longer-than-normal periods.
- Vaginal discharge that contains blood or is watery and smells strongly.
- Pain in the pelvis or during intercourse.
- The signs and symptoms of early-stage cervical cancer can also be signs of advanced cervical cancer, which means the cancer has spread to other parts of the body. ⁽²⁵⁾
- Bowel movements that are painful or difficult, or
- bleeding from the rectum during a bowel movement.
- Blood in the urine or difficult or painful urination.
- Legs getting bigger.
- An abdominal ache.



- Experiencing fatigue.

TREATMENT^(26,27,28,29,30)

➤ The patient's general health and the tumor's size, location, and stage all affect how cervical cancer is treated.

1. Surgery:

- Hysterectomy (uterine removal)
- Radical hysterectomy (removal of the uterus, cervix, and part of the vagina)
- Trachelectomy (removal of the cervix)
- Lymph node dissection (removal of lymph nodes)

2. Radiation therapy:

- Internal radiation therapy (brachytherapy)
- External beam radiation therapy (EBRT)

3. Chemotherapy:

1. Cisplatin: A chemotherapy medication based on platinum that is frequently used to treat cervical cancer.
2. Carboplatin: Another chemotherapy medicine based on platinum that is frequently used in conjunction with other drugs.
3. Paclitaxel: This chemotherapy medication, which is based on taxanes, is used to treat advanced cervical cancer.
4. Topotecan: A topoisomerase inhibitor used to treat cervical cancer that has returned or spread.

4. Targeted treatment:

The angiogenesis inhibitor bevacizumab (Avastin) targets the VEGF protein, which contributes to the formation of new blood vessels that provide cancer cells with nutrients.

2. The monoclonal antibody cetuximab (Erbix) targets the EGFR protein, which contributes to the development and spread of cervical cancer cells.

5. Immunotherapy includes:



1. Monoclonal antibodies, which are produced in a lab and target particular proteins on cancer cells to flag them for elimination.
2. Checkpoint Inhibitors: By releasing the immune system's brakes, these medications enable the body to more efficiently combat cancer cells.
3. Vaccines for cancer: These immunizations encourage the body to identify and combat cancerous cells. Adoptive T-cell therapy is a procedure in which the patient's T-cells are extracted, altered to identify cancer cells, and then reinfused into the patient.
5. Immuno modulators: These medications increase the production of cytokines by the immune system, aiding in the fight against cancer.
6. Palliative care: This type of treatment aims to improve the quality of life and relieve symptoms in patients with advanced or terminal cervical cancer.

Conclusion

Cervical cancer is still an important worldwide health concern, especially in places like India where high rates of morbidity and mortality are caused by a lack of knowledge, poor screening, and limited access to healthcare. The main reason, ongoing infection with high-risk HPV strains, emphasizes the value of immunization and early detection by routine screening programs like HPV testing and Pap smears. Hope for better results is offered by effective treatment methods, such as radiation, chemotherapy, surgery, and new immunotherapies, particularly when cancer is discovered early.

Reducing the burden of cervical cancer requires addressing inequalities in healthcare access, raising public awareness, and putting strong vaccine and screening programs into place. Governments, medical professionals, and communities working together can open the door to improved prevention, prompt diagnosis, and cutting-edge treatment alternatives. By giving these actions top priority, we can get closer to eradicating cervical cancer as a hazard to public health and enhancing women's lives everywhere.

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