



REVIEW ARTICLE

CERVICAL CANCER: A COMPREHENSIVE REVIEW

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Abstract

Since cervical cancer is the leading cause of cancer-related deaths among women in poor nations, efforts to prevent the illness using more modern methods and the HPV vaccine should be investigated. Most women in underdeveloped countries have advanced, frequently incurable cervical cancer, which has a very dismal prognosis. In contrast, early detection of cervical cancer is linked to great survival. A persistent infection with high-risk strains of the human papillomavirus (HPV) is the main cause of the aberrant cell development in the cervix that leads to cervical cancer. About 70% of instances of cervical cancer are caused by HPV types 16 and 18, out of more than 100 different varieties. Additional contributing variables include immunosuppression, smoking, multiple sexual partners, early initiation of sexual activity, and long-term use of oral contraceptives. Symptoms, when present, include abnormal vaginal bleeding (e.g., post-coital or intermenstrual), pelvic pain, and unusual vaginal discharge. Advanced stages may cause weight loss, fatigue, or pain during urination. Diagnosis typically involves a combination of Pap smear tests, HPV DNA testing, and colposcopy, with biopsy serving as a confirmatory method. Prevention strategies focus on vaccination and screening. HPV vaccines, such as Gardasil and Cervix, are highly effective in preventing infection from high-risk HPV types. Routine Pap smears and HPV testing facilitate early detection and removal of precancerous lesions. Safe sexual practices and smoking cessation also reduce risk. Treatment depends on the stage of the disease. Early-stage cervical cancer can often be cured with surgical methods like hysterectomy or conization.

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Introduction: -

Cervical cancer, a largely preventable disease, is one of the most common cancers found in women living in low- and middle-income countries [1]. One of the main causes of cancer-related deaths in women globally is cervical cancer, which epidemiologically behaves similarly to a venereal disease with minimal contagiousness. Early age at

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first intercourse and multiple sexual partners have been shown to exert strong effects on risk [2]. Cervical cancer is the fourth most frequent cancer in women worldwide, making it a serious global health concern. Depending on stage, histology, and patient factors, the standard management of cervical cancer is a combination of treatment approaches, including (fertility- or non-fertility-sparing) surgery, radiotherapy, platinum-based chemotherapy, and novel systemic therapies such as bevacizumab, immune checkpoint inhibitors, and antibody-drug conjugates [3]. In recent years, significant progress has been achieved in improving outcomes for recurrent metastatic cervical cancer. However, these advancements still fall short of addressing unmet patient outcomes needs. The development of immunotherapy and targeted therapies has shown promise for individuals with cervical cancer, offering new avenues for treatment. To enhance effectiveness, embracing innovative therapies and exploring combination treatment strategies is crucial. Additionally, centralizing care and encouraging participation in clinical trials remain vital to advancing treatment options and improving overall survival rates [4]. Cervical cancer often progresses slowly, starting as precancerous changes in the cervical tissue, known as cervical intraepithelial neoplasia (CIN). If left undetected or untreated, these changes can develop into invasive cancer.

DIFFERENT STAGES OF CARCINOMA

Stage I: Early-stage cancer: The cancer is limited to the cervix. The quantity of cancer is minimal and can only be seen under a microscope.

Stage II: The cancer has spread beyond the cervix: The cancer has spread beyond the cervix, but has not reached the lower third of the vagina or the pelvic wall. It has spread to the upper part of the vagina.

Stage III: Advanced cancer in the pelvic area: The cancer has extended to the lower third of the vagina, the pelvic wall, or has resulted in kidney issues. This encompasses the lower third of the vagina but excludes the pelvic wall.

Stage IV: distant spread (metastatic cancer): The cancer has spread beyond the pelvis to distant organs. It has spread to nearby organs, such as the bladder or rectum.

ETIOLOGY OF CERVICAL CANCER

Cervical cancer (CC) occurs due to the proliferation of abnormal cells in the cervix lining. The most prevalent form of CC is squamous cell carcinoma, representing 70% of occurrences. Adenocarcinoma is rarer and harder to identify as it originates higher in the cervix. In Australia, it is anticipated that 913 fresh cases of CC will be identified in 2021. High-and HPV vaccination for girls to support women. Precancerous lesions can be found early on by screening, when they are still treatable

[5]. Infections caused by different microorganisms trigger either the innate or adaptive immune response, potentially resulting in chronic inflammation that promotes pro-tumorigenic effects. Approximately 20% of cancers are linked to various microbial infections. Much evidence has confirmed that different pathogenic bacteria are linked with the growth of various types of cancer [6].

RISK FACTORS OF CERVICAL CANCER

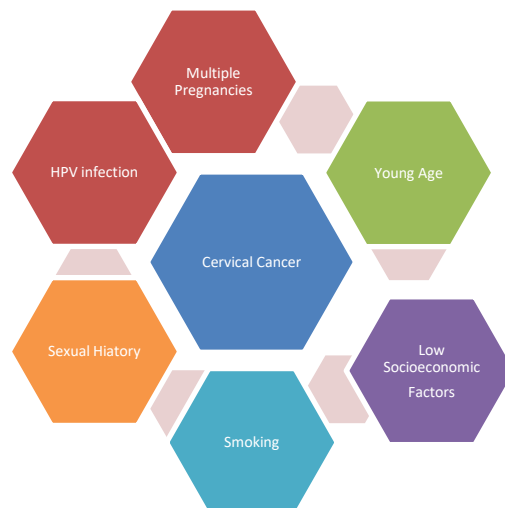


Figure 1: Risk factors of cervical cancer

Persistent infection with high-risk HPV is the primary factor contributing to the development and progression of cervical cancer, while other factors are thought to affect the likelihood of acquiring an HPV infection. While the mechanism associated with HPV-independent cervical cancer is unclear, the pathogenesis of HPV-associated cervical lesions and cancer is well-described [7]. The main cause of cervical cancer is a long-term infection with high-risk strains of the human papillomavirus (HPV). HPV is a sexually transmitted virus, and over 200 strains of HPV have been identified.

DIAGNOSIS OF CERVICAL CANCER

Cervical cancer is the second most common cancer in women worldwide, with more than half a million new cases diagnosed in 2005[8]. Currently, there are two types of diagnostic tests for cervical cancer screening: the Papanicolaou test and the HPV test. The first one detects precancerous and cancerous cell lesions to be effectively treated, and the second one detects infections by HPV types that could lead to cancer [9]. According to the most recent guidelines from the World Health Organization, three methods are recommended for early cervical cancer screening: HPV testing, cytology (such as the conventional Pap smear and liquid-based cytology), and visual inspection using acetic acid. Both HPV testing and cytology rely on cervical cell samples collected through brushing. Testing detects high-risk types of HPV infection in the cervix, whereas cytological examination uses a microscope to identify cells taken from the cervix for possible cervical cancer or precancerous lesions [10].

1. Pap Smear (Pap Testing)

This is a screening test where cells are collected from the cervix and examined for abnormal changes. Which could indicate cancer or precancerous conditions. The Pap test identifies potentially abnormal cervical cells by analysing the shape and structure of cell nuclei. Accurate diagnosis depends on automated systems and precise nucleus detection. Image databases have played a key role in developing these detection methods. This research aims to find out features by using computerised techniques to identify the shape, size, and structure of the cell nucleus [11].

2. HPV testing

Human papillomavirus (HPV) has been identified as an essential factor in the development of pre-invasive and invasive cancers of the lower genital tract, of which cervical cancer is the most prevalent [12]. The HPV testing process for cervical cancer involves collecting cervical cells during a pelvic exam using a small, soft brush or spatula. The sample is preserved in a liquid medium and sent to the laboratory, where molecular techniques, such as polymerase chain reaction (PCR) or hybrid capture 2, detect the presence of high-risk HPV strains. Often combined with a Pap smear for women aged 30 and older, this co-testing method increases the accuracy of screening. Results are interpreted as negative (no high-risk HPV found) or positive (high-risk HPV found), with follow-up testing such as genotyping, colposcopy, or biopsy performed if needed. HPV testing is an important tool for early detection and prevention, which, when paired with regular screening and HPV vaccination, can help prevent cervical cancer.

3. Colposcopy

Cervical cancer remains a major global health concern, with a particularly worrying incidence in young women. Traditional screening techniques, such as Pap smears and colposcopy, often lack sensitivity and specificity and are highly dependent on the experience of the gynecologist [13]. Colposcopy visit allows for modification of colposcopy procedures consistent with a woman's risk [14]. Colposcopy is a diagnostic technique used to closely inspect the cervix for indications of cervical cancer or early precancerous abnormalities. During the procedure, the patient lies on an examination table, and a speculum is inserted into the vagina to expose the cervix. A colposcope, a lighted magnifying instrument, is placed outside the vagina to provide a detailed view of the cervical tissues. The doctor may apply acetic acid (vinegar) or iodine to highlight abnormal areas. If suspicious areas are identified, a small biopsy (tissue sample) may be taken for further examination under a microscope. Colposcopy is a safe and effective way to evaluate abnormal Pap smear results or positive HPV tests and helps guide further treatment or monitoring.

4. Biopsy

A cervical biopsy is a procedure in which a small sample of cervical tissue is removed for further examination to detect cancer or precancerous changes. It is typically performed after abnormal Pap smear results, a positive HPV test, or suspicious findings during colposcopy. During the procedure, the patient lies on an examination table, and a speculum is used to view the cervix. A local anesthetic may be applied to minimize discomfort. Depending on the area of concern, different types of biopsies may be performed, such as punch biopsy (removing small tissue samples with a biopsy instrument), endocervical curettage (removing cells from the cervical canal), or cone biopsy

(removing a larger, cone-shaped section of tissue). The samples are sent to a laboratory for microscopic analysis to detect the presence of abnormal or cancerous cells. The procedure is usually quick, with minor cramping or spotting common afterward.

SYMPTOMS OF CERVICAL CANCER:

Cervical cancer does not show obvious symptoms in the early stages. However, as the disease progresses, the following symptoms may appear. Unusual vaginal discharge: Watery, bloody, or foul-smelling discharge. Unusual vaginal bleeding may include bleeding between menstrual periods, after sexual activity, or following menopause. Pelvic pain refers to discomfort or aching in the lower abdominal area that is unrelated to the menstrual cycle. Pain during intercourse: Also known as dyspareunia. Difficulty urinating or changes in bowel habits: Blood in urine or stool. Pain during urination. Constipation or changes in bowel movements. Lower back pain: Persistent pain that may radiate to the legs. Unexplained weight loss: Rapid or unintended weight loss. Fatigue, Leg swelling: Persistent tiredness and lack of energy. Swelling in one or both legs due to lymphatic obstruction.

PREVENTION, AND CURE

There are two ways to control the incidence of cervical cancer. One way is to prevent precancers in the first place, and the other is to detect precancers before they become actual cancers. Prevention of HPV infection is key to preventing cervical cancer; however, there is not one solution to prevent infection with all the different types of HPV. Secondary prevention strategy for some cancers [15]. Although awareness of cervical cancer and its screening methods was widespread, understanding of HPV and the actual rate of screening remained low, even though many expressed a strong willingness to undergo screening. Increased investment in education and awareness campaigns, as well as an organised cervical cancer screening programme, are needed to promote screening and reduce the burden of cervical cancer in Uganda [16]. Cervical cancer is preventable through screening and vaccination methods; however, access to these preventive measures is limited nationally and globally, and thus, many women will still develop cervical cancer [17]. Antioxidants and nutrition involve vitamins E, D, C, and A, which have a remarkable role in the prevention of cervical cancer. The six HPV vaccines available worldwide protect against the high-risk types 16 and 18, which prevent most cervical cancers. The ideal timing of vaccination is 1 or 2 doses for girls aged 9-14 years; 2 or 3 doses for girls with compromised immunity [18]. Diagnosis can be made by cytological examination of exfoliated cervical cells. Persistent infection is the best predictor of cervical cancer risk [19]. The association between cervical cancer screening and incidence is stronger in more advanced cancers, and screening is more effective at preventing cancer deaths than at preventing cancer [20].

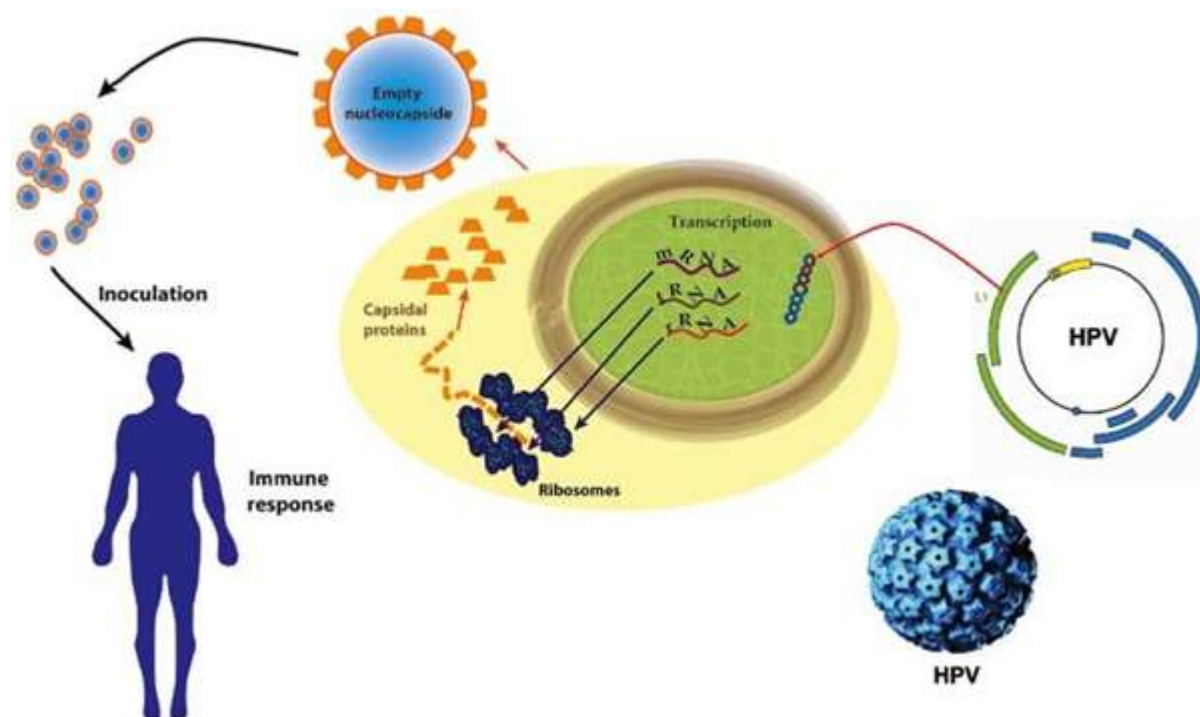


Figure 2: The mechanisms of action of HPV vaccines. [21]

Conclusion: -

Cervical cancer continues to pose a major global health challenge, especially in low-resource settings where access to comprehensive screening and vaccination programs remains limited. The primary cause of cervical cancer is a persistent infection with high-risk strains of the human papillomavirus (HPV), particularly HPV types 16 and 18. These infections are often asymptomatic in the early stages, allowing the virus to persist and potentially cause cellular changes that may progress to cancer if left untreated. Additional risk factors such as smoking, immunosuppression (including HIV infection), and co-infections with other sexually transmitted infections can further increase the likelihood of disease development. Early diagnosis plays a crucial role in improving outcomes, as it allows for the detection of pre-cancerous lesions before they evolve into invasive cancer. Screening methods such as Pap smears, HPV DNA testing, and colposcopy have proven to be highly effective in identifying these early cellular abnormalities, thereby significantly reducing mortality rates associated with the disease. Unfortunately, many women in underserved areas only present symptoms such as abnormal vaginal bleeding, pelvic pain, or unusual vaginal discharge when the cancer has already reached an advanced stage, at which point treatment becomes more complex and less successful. Therefore, prevention is key, and the most effective strategies include the widespread administration of HPV vaccines, which have demonstrated high efficacy in preventing infection with the most dangerous HPV strains, and the implementation of regular cervical screening programs. These measures, coupled with public education campaigns to raise awareness about cervical cancer risks and symptoms, and efforts to improve access to healthcare services, can significantly reduce the burden of this largely preventable disease.

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