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Cervical Cancer: Disease prevalence,Risk Factors, Pathophysiology, Newer modalities of Screening and Management

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ABSTRACT:

Cervical cancer stands as the second most prevalent cancer affecting women globally, particularly impacting regions with lower economic means. In India, it remains the leading malignancy among women for the past two decades, with its highest occurrence seen in women aged 55 to 59. The National Cancer Registry Programme (NCRP) indicates that breast and cervical cancers are the most common malignancies in females. Human Papillomavirus (HPV) infection plays a significant role in cervical cancer development, especially in women without other gynecological issues. Socioeconomic factors such as low income, limited education, and higher parity contribute to increased vulnerability.In developed countries like the United States, screening efforts primarily involve HPV testing and Pap smears, which detect abnormal cytology and HPV exposure. Lifestyle factors such as early sexual activity, multiple partners, menstrual hygiene practices, and lack of protection during sexual encounters are closely associated with cervical cancer incidence. Prevention strategies include health education, behavioral interventions, legislative actions, and encouraging better healthcare-seeking behaviors.Cervical cancer is largely preventable through primary prevention methods and screening, which significantly reduce the burden of the disease and mortality. Global collaboration is essential to achieve the 90-70-90 objectives by 2030, aiming to eliminate cervical cancer. This concerted effort is crucial for the long-term eradication of the disease.

INTRODUCTION:

Cervical cancer, originating in the cervix, is predominantly caused by prolonged infections of high-risk HPV types. The majority of sexually active individuals will encounter an HPV infection at some point. Thankfully, in most cases, the body's immune response clears the infection within 1-2 years, preventing cancerous developments. However, persistent infections with high-risk HPV strains can lead to changes in cervical cells, potentially progressing to cervical cancer if not addressed promptly.[1]

Those who initiate sexual activity at an early age, particularly before 18, or engage in multiple sexual partners, face an increased risk of contracting high-risk HPV variants. There are over 100 HPV variants, with at least 14 known to be carcinogenic. Notably, HPV type 16 is responsible for 55-60% of cervical cancer cases, while HPV type 18 accounts for 10-15%. The remaining cases are attributed to roughly 10-15 other HPV types.[2] These cancer-causing HPVs are primarily transmitted through sexual activity and direct genital contact. Fortunately, the body clears around 90% of HPV infections within 1-2 years. However, persistent HPV infections can lead to the formation of precancerous conditions known as Cervical Intraepithelial Neoplasia (CIN). CIN is categorized into varying grades: CIN1 denotes early-stage,

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CIN2/3 signifies more advanced stages, and CIN3+ marks the presence of invasive cancer.[1]
Persistent HPV infections, especially high-risk variants, for over 2 years indicate a likelihood of CIN2/3, and beyond 5 years, a potential risk of CIN3+ at a rate of 20-30%. Without intervention, cervical cancer typically develops within 15-20 years for women with regular immune function and within 5-10 years for those with compromised immunity, such as individuals with untreated HIV.[3] The chances of regression to normalcy are 57% for CIN1, 43% for CIN2, and 32% for CIN3. Alarmingly, over half of all cervical cancer cases are detected in unscreened women, with 10% identified in those who haven't undergone screening in the past 5 years.[4] This article aims to review the prevalence, risk factors, pathophysiology, newer modalities of screening, and management of cervical cancer.

Disease Prevalence And Secular Trends: According to the Global Cancer Statistics for 2020, cervical cancer remains the second most common cancer among women worldwide. In that year, there were 604,000 new cases reported globally, resulting in 342,000 deaths.[5] Cervical cancer is the most frequently diagnosed cancer in 28 countries and is the leading cause of cancer-related deaths in 42 countries. It is particularly prevalent in South-Eastern Asia and Sub-Saharan Africa, where it ranks as the most common cancer and the primary cause of cancer-related mortality in some regions.[6]
In lower-income settings, cervical cancer ranks second in both incidence and mortality, following breast cancer. India carries the largest burden of cervical cancer patients globally, with 123,907 new cases reported in 2020, accounting for 23% of global cervical cancer deaths.[7] Approximately 6–29% of all female malignancies in India are attributed to cervical cancer. The age-adjusted incidence rate in India varies significantly, ranging from 4.91 to 23.07 per 100,000 individuals.[8]
Notably, there has been a threefold increase in cervical cancer incidence in countries with lower Human Development Index (HDI) compared to those with very high HDI. Cervical cancer-related deaths are six times higher in countries with lower HDI, indicating slow progress in reducing the burden of cervical cancer in most low and middle-income countries (LMICs).[9]
The age-standardized incidence of cervical cancer is lowest in western Asia, while mortality rates mirror this pattern, with the highest rates observed in eastern Africa and the lowest in western Europe. Countries such as Bulgaria and Romania in central and eastern Europe report relatively high mortality rates.[10]
Regionally, Asia has the highest estimated proportion of cervical cancer cases (58%), followed by Africa (20%), Latin America (10%), and Europe (10%).[11] A significant number of mortalities occur in Asia (58%), Africa (22%), and Latin America (9%), with China and India accounting for 39% of all cases. These statistics underscore the urgent need for targeted interventions and improved access to screening and treatment programs, particularly in regions with high disease burden.[12]

Risk Factors:
Exposure to HPV is associated with numerous risk factors for cervical cancer. The development of invasive cancer after an HPV-related precursor lesion can take up to two decades. However, various factors such as early sexual activity (before the age of 16 or with multiple partners), smoking, high parity, and residing in socioeconomically disadvantaged areas may increase the likelihood of developing cervical cancer.[13] Human immunodeficiency virus In individuals with HIV (human immunodeficiency virus), high-risk strains of HPV are more likely to infect women. Research on the link between HIV and cervical cancer indicates that HIV-positive individuals face higher risks of CIN, invasive cervix carcinoma, abnormal Pap smear results, and chronic HPV infection with various oncogenic viruses.[14] HIV-positive women also exhibit an increased risk of HPV infection at a younger age (13-18 years) and a heightened susceptibility to cervical cancer. Notably, cervical cancer is detected earlier in HIV-positive women (aged 15-49 years) compared to those who are not infected.[15] Chlamydia Trachomatis In a study conducted by Koskela et al.[16], it was found that prior infection with Chlamydia trachomatis contributes to an elevated risk of cervical squamous cell carcinoma. The study reported the detection of C. trachomatis DNA in 40% of invasive squamous cell carcinoma cases. Another case-control study spanning seven countries revealed that serum antibodies against C. trachomatis are associated with a 1.8-fold increase in the risk of squamous cell carcinoma, particularly in women with higher antibody titers and those under 55 years of age. It is suggested that C. trachomatis infection may heighten the risk of squamous cell carcinoma by increasing susceptibility to HPV or augmenting HPV-mediated effects. The chronic inflammation resulting from C. trachomatis infection can lead to the generation of reactive oxygen species, potentially damaging DNA and raising the risk of

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HPV-associated carcinogenesis. Additionally, women infected with C. trachomatis may experience compromised ability to clear HPV infections (Smith et al., 2004)[17]. Chlamydia infection can induce chronic inflammation, cervical hypertrophy, and squamous metaplasia, with metaplastic cells becoming potential targets for HPV.[18] Sexual partner Cervical cancer has been associated with factors related to sexual behavior. Research indicates that women with multiple sexual partners are at an increased risk of developing cervical cancer. Additionally, numerous studies have shown that having frequent sexual partners raises the likelihood of HPV infection and cervic l cancer in women. Early age at first sexual intercourse is another risk factor for cervical cancer.[19]

Oral contraceptive pills

The use of Oral Contraceptive (OC) medications is associated with an increased risk of cervical cancer. A global collaborative epidemiological study on cervical cancer revealed that prolonged use of OCs was linked to a higher relative risk among current users.[20] Several studies have demonstrated that using OCs for at least five years elevates the risk of developing cervical cancer.[21] Furthermore, in a multi-center case-control study, women testing positive for HPV DNA had a threefold greater likelihood of cervical cancer if they had used OC pills for five years or more.[22] Notably, adenocarcinoma, a specific type of cervical cancer, was particularly associated with OC pill usage, as indicated by a recent meta-analysis and comprehensive review.

Multiple pregnancies

Several additional studies have suggested that the link between multiple pregnancies and cervical cancer might stem from the higher prevalence of cervical anomalies in pregnant women, possibly due to endocervical migration during pregnancy.[23] Other theories propose that the positive correlation between cervical cancer and parity could be attributed to injuries sustained by the uterine cervix during vaginal delivery. Contrary to common assumptions, cesarean deliveries are not as strongly associated with cervical cancer as vaginal deliveries, implying that injuries incurred during vaginal deliveries may contribute to increased risks.[24]

Smoking

Research indicates that smoking reduces the local immune response and induces mutagenic effects on cervical cells, potentially facilitating the persistence of HPV or leading to cancerous alterations in the cervix.[25] Smoking emerges as the primary risk factor for high-grade cervical lesions not attributed to HPV infection. Conversely, there appears to be minimal or no association between smoking and low-grade cervical lesions.[26]

Herpes Simplex Virus (HSV)

According to Smith et al., there appears to be an association between serum HSV-2 antibodies and invasive cervical cancer, including squamous cell carcinoma, adenocarcinoma, or adeno-squamous cervical carcinoma.[27] However, these findings have not been substantiated. For example, a nested case-control study conducted by Lehtinen et al.[28] concluded that HSV-2 does not contribute to cervical carcinogenesis.

Obesity

Obesity is linked to an increased risk of cervical carcinoma, particularly adenocarcinoma, which is influenced by hormonal factors. Studies by Lacey et al.[29] (2003), Lee et al.[30] (2013), and Poorolajal and Jenabi[31] (2016) highlight this association. In a case-control study, obese women with a body mass index (BMI) of 30 or higher and overweight women with a BMI of 25 or higher were found to have a twofold higher risk of developing cervical adenocarcinoma compared to other women (Lacey et al.[29], 2003).

Obese women are less inclined to undergo cervical cancer screening (Ludman et al.[32], 2010; Wee et al.[33], 2000). Several factors contribute to lower screening rates in this demographic. Obese women may experience delays in accessing healthcare services due to body image concerns, feelings of shame, reduced provider respect, and reluctance to address weight concerns (Friedman et al.[34], 2012).

Human papilloma virus

The human papillomavirus is a collection of different DNA viruses . More than 200 different types of human papillomavirus (HPV) have been identified to date. HPV infections can lead to various cancers, including cervical, vaginal, anal, vulvar, and oral cancers. Both males and females can be affected by HPV infections. In males, HPV can cause oropharyngeal and penile cancer, while in females, it is associated with cervical, vaginal, and oral cancers. Additionally, HPV infections can result in genital warts, characterized by their cauliflower-like appearance. HPV is classified into high-risk and low-risk types based on its potential to cause cancer.[1] (Table 1)

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Table 1: High risk and low risk strains of human papilloma virus

Human papilloma virus	strains
High risk human papilloma viruses	39,16,45,18,51,31,52,33, 56,35,58,59,68
Low risk human papilloma viruses	42,43,44

Human papillomavirus (HPV) 16 and 18 are oncogenic, stimulating cellular proliferation by disrupting control mechanisms. Increased sexual activity raises the likelihood of HPV infection. Individuals with multiple sexual partners, or whose partners have had multiple partners, as well as those engaging in early sexual activity, are at higher risk of acquiring the infection.[1]

Nutrition and Dietary Factors

The role of nutritional factors in cervical cancer pathogenesis has garnered significant attention in recent years, with several studies exploring this area, albeit yielding conflicting results (González et al.[35], 2011; Labani et al.[36], 2009; Siegel et al.[37], 2010). In one study, increased concentrations of α- and γ-tocopherol and higher dietary intake of green vegetables, dark green, and yellow fruits were associated with a 50% decrease in CIN 3 (Tomita et al.[38], 2010), indicating that a healthy and balanced diet may elevate antioxidant levels and potentially influence cervical neoplasia. Additionally, Ghosh et al.[39] (2008) found a significant correlation between higher intake of vitamin C, folate, vitamin E, beta-carotene, vitamin A, lycopene, and vegetarian foods with cervical cancer risk.

Inflammatory Disease

Multiple studies have explored the connection between inflammatory diseases and cervical cancer (Bernatsky et al.[40], 2009; Kiss et al.[41], 2010; Simon et al.[42], 2015). Findings from a population-based cohort study revealed that women with rheumatoid arthritis and systemic lupus erythematosus face a 1.5-fold increased risk of developing cervical dysplasia and cervical cancer (Kim et al.[43], 2014). A meta-analysis further demonstrated a positive correlation between systemic lupus erythematosus and the risk of cervical neoplasia, indicating that individuals with this condition are at a heightened risk of cervical cancer (Liu et al.[44], 2010). For example, Al-Sherbeni et al.[45] (2015) found a higher rate of abnormal Pap smears in patients with lupus. Additionally, it has been observed that the use of immunosuppressive agents, such as cyclophosphamide and azathioprine, may contribute to an increased incidence of cervical cancer in these individuals. Conversely, the screening rate for cervical cancer tends to be lower among people with lupus.

PATHOPHYSIOLOGY: The development and progression of cervical cancer are significantly influenced by dysregulation of the cervical microbiota by human papillomavirus (HPV), modulation of the immune response, and the emergence of new mutations causing genomic instability. Additionally, viral infections such as Epstein-Barr virus, Hepatitis B and C viruses, and human herpesvirus contribute to cervical cancer by interfering with cellular regulatory proteins, inactivating tumor suppressor genes, evading host immune responses, inducing persistent inflammatory responses, triggering epigenetic modifications, stimulating angiogenesis, and activating telomerase. Dysregulation of genes like cyclin-dependent kinase inhibitor 2A (CDKN2A), SRY-box 17 (SOX17), and checkpoint kinase 1 (CHEK1) further promotes cancer cell growth by disrupting DNA repair mechanisms and apoptosis due to HPV genome integration into host chromosomes and inactivation of tumor suppressor proteins p53 and retinoblastoma (pRb).[46]

Prognostic factors for cervical cancer include the number of retrieved lymph nodes, age at symptom onset, use of a uterine manipulator during laparoscopic surgery, and the combination of retrieved lymph node count and FIGO staging system. Patients with a higher number of retrieved lymph nodes experience significantly better progression-free survival (PFS). Younger patients (aged 25 to 39) at symptom onset have a poorer prognosis, whereas laparoscopic therapy using a uterine manipulator is associated with a better prognosis. Combining the retrieved lymph node count with the FIGO staging method enhances the prediction of PFS, serving as potential predictors of cervical cancer prognosis.[47]

Portable colposcopy equipment holds promise for enhancing cervical cancer screening, particularly in low- and middle-income countries (LMICs). Studies have demonstrated its diagnostic test accuracy (DTA) in identifying cervical intraepithelial neoplasia grade 2 or higher (CIN2+), with pooled sensitivity of 0.79 and specificity of 0.83 when combined with other tests.[47]

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SIGNS OF CERVICAL CANCER

Detecting cervical cancer can be challenging as it often shows no early signs. Symptoms typically manifest only after the cancer has begun to spread. However, some indicators of early-stage cervical cancer include:

- Vaginal bleeding after intercourse
- Vaginal bleeding after menopause
- Irregular vaginal bleeding between periods, along with heavier or longer-than-usual menstrual cycles
- Pelvic discomfort or pain during sexual intercourse[48]
-

SYMPTOMS OF CERVICAL CANCER

Initially, individuals with cervical cancer may not exhibit any symptoms. Precancerous cervical cancer is typically only detectable through abnormalities found in a biopsy or Pap smear. Additional symptoms include irregular vaginal bleeding, bleeding during sexual intercourse, heavy menstrual bleeding, pelvic pain spreading from the leg to the back, and abnormal vaginal discharge. The abnormal vaginal discharge can be attributed to either human papillomavirus infection or the cancer itself.[49]

The staging process considers factors such as the cancer's location, extent of spread, and potential impact on other body parts. cervical cancer is being staged according to the system developed by the International Federation of Obstetrics and Gynecology (F.I.G.O.). This assessment relies on clinical examination findings, radiological imaging, and biopsy results.

Stage I: In this initial phase, cancer is limited to the uterus, originating from the cervical lining and infiltrating deeper tissues. There is no evidence of its presence in other anatomical sites. This stage can be further subdivided for a more detailed description of the cancer's progression.

Stage II: Progression to this stage involves the extension of cancer beyond the uterus, affecting adjacent regions such as the vaginal canal and cervical tissue. However, its spread remains confined to the pelvic region, without indication of spreading to other parts of the body.

Stage III: The tumor's advancement leads to infiltration into the pelvic wall, potentially causing the enlargement of one or more kidneys (hydronephrosis). It may also impact kidney function and involve nearby lymph nodes. This stage is characterized by the tumor's spread to a more extensive extent.

Stage IV: At this stage, while cancer has not yet spread to distant body parts, its influence extends to the bladder and rectum, highlighting its advanced nature within the pelvic region.[49]

SCREENING AND PREVENTION:

Primary prevention of cervical cancer with HPV vaccination:

The cross-sectional prevalence of HPV varies with age, peaking at 25% among women under 25 years old. This indicates that HPV transmission primarily occurs through sexual activity following sexual debut. Therefore, to prevent HPV infection, prophylactic vaccination should aim at girls aged 10–14 years, prior to the onset of sexual activity. (Bhatla et al.[50], 2021). HPV vaccination has been available since 2006 and is accessible in many countries worldwide, although vaccine coverage varies significantly across regions (Herrero et al.[51], 2015). Sociocultural, health, and political factors present the main barriers to vaccine uptake, particularly in low-income and less developed countries (Wigle et al.[52], 2013).

Currently, there are three types of vaccines available:

- Quadrivalent vaccine (Gardasil): Comprising viral-like particles of the L1 recombinant protein (major capsid protein) targeting HPV types 6, 11, 16, and 18 (Siddiqui and Perry[53], 2006).
- Bivalent vaccine (Cervarix): Containing viral-like particles of recombinant L1 capsid proteins targeting HPV types 16 and 18 (Monie et al.[54], 2008).
- Nonavalent vaccine: Approved by the US Food and Drug Administration (FDA) in December 2014 and the European Medicines Agency in June 2015, this vaccine includes HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58. It offers nearly 90% protection against cervical cancer and approximately 90% protection against genital warts (Bonanni et al.[55], 2017).

These vaccines primarily safeguard individuals against the HPV types included in the vaccine and provide limited protection against other HPV types. They are recommended for both women and men aged nine and older, administered in two doses. For individuals over 15 years of age, three vaccine shots are typically given.

Secondary prevention of cervical cancer:

During cervical cancer screening, human papillomavirus (HPV) infection is detected to

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identify precancerous lesions or malignancies. Treatment is administered if necessary. Screening is typically conducted on healthy, asymptomatic women. If precancerous lesions or HPV infection are detected during screening, immediate treatment can be provided to prevent cancer progression. Early detection through screening enhances the likelihood of successful treatment.[56]

The World Health Organization (WHO) recommends governments to utilize HPV testing methods such as HPV genome sequencing and HPV mRNA assays for cervical screening. High-risk HPV strains are commonly associated with cervical cancer, and HPV-DNA testing can identify these strains. HPV mRNA testing detects cellular changes following HPV infection. HPV screening is an objective test, offering advantages over subjective methods such as visual inspection. It is more effective, saves lives, and detects more cancer and precancerous lesions.[56] Moreover, it is cost-effective compared to cytology-based methods like pap smears. Routine HPV testing every 5 to 10 years is recommended for women in the general population starting at age 30. HIV screening should commence at age 25, with annual screening for HIV-positive women becoming the new standard. Both cervical cytology and HPV testing involve collecting samples from the cervix, although WHO suggests using self-collected samples for HPV DNA testing (excluding HPV mRNA tests) to improve accessibility and comfort for women. Proper support is essential for women to feel comfortable with the procedure.Treatment and management of positive screening test results should be linked to screening programs. Women who test positive for HPV may receive treatment without a formal diagnosis in resource-limited settings. Triage tests, such as VIA, are necessary to identify HPV-positive women before treatment, especially for HIV-positive women.[56]

STAGING OF CERVICAL CANCER:

In 1958, FIGO (International Federation of Gynecology and Obstetrics) established the first clinical staging system for cancer, focusing on the cervix. Later, the TNM (Tumor, Node, Metastasis) staging system was introduced to document nodal and metastatic disease status. In 2018, the FIGO Gynecologic Oncology Committee updated the staging process, allowing for the utilization of clinical, radiological, or pathological findings, depending on availability, to determine the stage. A subsequent corrigendum was published with adjustments to this staging system.[50]

The FIGO staging system for cervical cancer, updated in 2018, is as follows:

Stage 0: Carcinoma in situ (preinvasive carcinoma)
Stage I: Cancer confined to the cervix
IA: Invasive carcinoma diagnosed only by microscopy
IA1: Measuring 5 mm or less in greatest dimension
IA2: Measuring more than 5 mm but not more than 7 mm in greatest dimension
IB: Clinical lesions confined to the cervix or preclinical lesions greater than Stage IA
IB1: Clinically visible lesion 4 cm or less in greatest dimension
IB2: Clinically visible lesion more than 4 cm in greatest dimension
Stage II: Cancer extending beyond the cervix but not reaching the pelvic wall or involving the lower third of the vagina
IIA: No obvious parametrial involvement
IIB: Obvious parametrial involvement
Stage III: Cancer extending to the pelvic wall and/or involving the lower third of the vagina and/or causing hydronephrosis or nonfunctioning kidney
IIIA: Tumor involves the lower third of the vagina with no extension to the pelvic wall
IIIB: Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney
Stage IVA: Cancer invading the mucosa of the bladder or rectum and/or extending beyond the true pelvis
IVA1: Invasion of the mucosa of the bladder or rectum
IVA2: Extension beyond the true pelvis
Stage IVB: Distant metastasis

This staging system allows for the inclusion of clinical, radiological, or pathological findings to determine the stage, depending on availability.[50]

DIAGNOSIS:

Cervical cancer diagnosis encompasses a wide array of techniques. Traditional methods like the Pap smear involve examining cervical cells under a microscope to detect abnormalities. Visual inspection with acetic acid (VIA) is another conventional technique utilizing acetic acid to identify abnormal areas on the cervix. More recent advancements include HPV testing, which detects the presence of high-risk HPV genotypes.[57] Other diagnostic techniques include:

Bimanual pelvic examination and sterile speculum examination: These involve manually feeling the pelvic area for abnormalities and visually inspecting the cervix, vagina, and external genitalia.

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Colposcopy: A specialized magnifying tool used to closely examine the cervix, vagina, and vulva for cancerous or precancerous growths.
Portable colposcopy: Provides quick screening results and is being explored for automation through computer vision and machine learning algorithms.
Various other methods such as biopsy, pelvic examination, imaging scans (CT/CAT scan, MRI, PET), biomarker testing, and endoscopic procedures (cystoscopy, sigmoidoscopy) are also utilized in diagnosis.
In low- and middle-income countries (LMICs), diagnostic methods like the Xpert HPV test, visual inspection with Lugol's iodine (VILI), conventional Pap smear, and urine-based HPV testing are used due to their affordability.[57]

MANAGEMENT: Comprehensive guidelines encompassing diagnosis, therapy, follow-up, quality of life, long-term survivability, and palliative care form an integral part of managing cervical cancer. To ensure consistency in patient care across different stages of cervical cancer, a management guide wheel has been developed based on recommendations from leading organizations such as the National Comprehensive Cancer Network (NCCN), the Society of Gynecologic Oncology (SGO), and the European Society of Gynecological Oncology (ESGO).[58]
Treatment for cervical cancer typically involves a combination of techniques including surgery, radiation therapy, and chemotherapy. Surgery may be utilized in specific cases such as the management of enlarged lymph nodes or metastases.It is a suitable treatment option for early stages of cervical cancer, such as Stage IA1 and Stage IA2. For Stage IA1, cervical conization is typically recommended, unless there are indications of lymphovascular space invasion (LVSI) or tumor cells at the surgical margin. In cases where childbearing is completed or in older women, extrafascial hysterectomy may also be considered. Various surgical routes, including abdominal, vaginal, or minimally invasive approaches, can be utilized.[50]
In Stage IA2 cases, due to a small risk of lymph node metastases, pelvic lymphadenectomy is often performed along with type B radical hysterectomy. For low-risk cases without LVSI and negative sentinel nodes, simpler surgical approaches like simple hysterectomy or trachelectomy, coupled with pelvic lymphadenectomy or sentinel lymph node assessment, may suffice. In cases where fertility preservation is desired, options may include cervical conization with pelvic lymphadenectomy or radical trachelectomy, performed through abdominal, vaginal, or minimally invasive methods.[50]
For the treatment of Stage IB1, IB2, and IIA1 lesions, surgical intervention is typically the preferred approach. This commonly involves performing a type C radical hysterectomy alongside pelvic lymphadenectomy. In cases categorized as FIGO Stage IB1, which are deemed low risk due to criteria such as less than 50% cervical stromal invasion and absence of suspicious lymph nodes on imaging, the standard treatment approach involves a type C radical hysterectomy. However, in such instances, a modified radical hysterectomy may also be considered. Pelvic lymphadenectomy is consistently recommended due to the high likelihood of lymph node involvement.[50]
For cervical cancer classified as FIGO Stages IB2 and IIA1, the primary treatment option can be either surgery or radiotherapy, depending on various patient factors and local resource availability. Both treatment modalities yield comparable outcomes.[50]
In cases of Stages IB3 and IIA2, where tumors tend to be larger and the chances of high-risk factors such as positive lymph nodes, positive parametria, or positive surgical margins are elevated, increasing the risk of recurrence, the choice of treatment modality must be carefully considered. This decision should take into account factors such as resource availability, as well as tumor- and patient-specific characteristics. Concurrent platinum-based chemoradiation (CCRT) emerges as the favored treatment approach for lesions falling within Stages IB3 to IIA2.[50]
In rare instances, patients diagnosed with Stage IVA disease may exhibit solely central involvement without extending to the pelvic sidewall or distant areas. In such scenarios, or in the event of recurrence presenting similarly, the option of pelvic exenteration may be contemplated, although it typically carries a bleak prognosis.[50]
In situations where surgery or anesthesia is not feasible due to contraindications, radiotherapy offers comparable outcomes in terms of local control and survival. Treatment decisions should be based on clinical, anatomical, and social considerations. For patients with microinvasive disease, intracavitary radiation therapy (ICRT) alone has shown promising outcomes when surgery is ruled out due to medical reasons. Additionally, selected individuals with very small Stage IB1 disease (less than 1 cm) may receive ICRT alone,

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especially if there are relative contraindications to external beam radiation therapy (EBRT). Typically, a dosage of 60–65 Gy equivalent is prescribed to Point A. Alternatively, a combination of EBRT and ICRT remains an option for such patients.[50]

The necessity of vaginal brachytherapy remains uncertain; nevertheless, it might be contemplated for patients displaying close or positive margins, sizable or deeply penetrating tumors, involvement of the parametrium or vagina, or extensive lymphovascular space invasion (LVSI). Vaginal cuff brachytherapy typically involves the placement of ovoids or cylinders in the upper one-third of the remaining vagina and should consist of two weekly fractions of high dose rate (HDR) brachytherapy, each delivering 6 Gy prescribed to 5 mm from the surface of the vaginal cylinder/ovoid.[50] With advancements in brachytherapy and external beam radiation contributing to improved patient outcomes and reduced toxicity. Chemotherapy, including neoadjuvant regimens, has shown benefits in reducing tumor size and pathological risk factors, particularly in patients with locally advanced disease.[59] Colposcopy serves as a crucial tool for identifying and treating preinvasive lesions and cervical cancer. It helps to detect abnormalities, confirm diagnoses, and guide appropriate care. Recent updates in colposcopic terminology provided by the International Federation of Cervical Pathology and Colposcopy have enhanced the accuracy of the procedure. Women with cytological indications of high-grade lesions should be promptly referred for colposcopy and biopsy.[60] Overall, colposcopy plays a vital role in cervical cancer prevention, early detection, and treatment strategies, complementing cervical cancer screening and HPV vaccination efforts. However, low- and middle-income countries (LMICs) face significant challenges in timely and effective management of cervical cancer due to limited resources, including prolonged treatment wait times, inadequate record-keeping, restricted access to pathology and radiotherapy services, and insufficient awareness and knowledge about cervical cancer and screening programs.[60]

CONCLUSION:

Highlighting the significant global health impact of cervical cancer, which affects women worldwide, is crucial. Human papillomavirus (HPV) is the primary cause of cervical cancer, emphasizing the importance of understanding its manifestations and indicators for women's health. Recognizing symptoms such as discomfort during sexual activity, pelvic sensations, and abnormal vaginal bleeding is essential for early detection and timely intervention. Cervical cancer is classified into stages based on the severity of the condition and the extent of cell spread, underscoring the importance of early detection through screening tests like Pap smear and HPV test, which significantly improve treatment outcomes. Preventive measures such as HPV vaccination, practicing safe sex, and regular checkups can help prevent cervical cancer. Women should prioritize their health and take necessary steps to prevent or detect cervical cancer early. With early detection and effective treatment, the prognosis for cervical cancer can be favorable.

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