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THE REVIEW ON MANAGEMENT OF CERVICAL CANCER

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Abstract
Cervical cancer is a major cause of morbidity and mortality among women worldwide, particularly in low- and middle-income countries. Persistent infection with high-risk human papillomavirus (HPV) types, notably HPV-16 and HPV-18, is the primary etiological factor, leading to molecular and cellular alterations that drive malignant transformation. Additional risk factors include immunosuppressant, early sexual activity, multiple sexual partners, smoking, and genetic susceptibility. Early-stage disease is often asymptomatic, emphasizing the importance of regular screening through Pap smears, HPV DNA testing, or visual inspection with acetic acid. Common clinical manifestations include abnormal vaginal bleeding, pelvic pain, vaginal discharge, urinary and gastrointestinal symptoms, and systemic features such as fatigue and weight loss in advanced cases. Strategies for management vary depending on the stage. The main treatment for early-stage cervical cancer is surgery, such as radical hysterectomy or fertility-sparing operations, sometimes in conjunction with adjuvant chemoradiation. Concurrent chemo radiation is used to treat locally advanced illness, usually with regimens based on cisplatin. Systemic chemotherapy, targeted therapy, and immunotherapy—including immune checkpoint inhibitors and anti-angiogenic drugs-may be necessary for recurrent or metastatic cervical cancer. In addition to early identification through screening programs, prevention through HPV vaccine, safe sexual practices, and lifestyle adjustment is still crucial. The future of precision oncology in cervical cancer is represented by emerging treatments such therapeutic vaccines, targeted medicines, and customized genetic techniques. To lower the burden of disease and enhance patient survival and quality of life worldwide, a multidisciplinary strategy incorporating prevention, early diagnosis, effective treatment, and follow-up is crucial.

Keywords: Cervical cancer, Human Papillomavirus (HPV), Chemoradiation, precisionOncology, Immunotheraphy.

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INTRODUCTION

Definition:

Management of cervical cancer is the set of medical steps taken to prevent, detect, treat, and follow up women with cervical disease. It includes prevention (mainly HPV vaccination), screening to find precancerous changes early, treatment options such as surgery, radiotherapy, chemotherapy and newer targeted or immune therapies for established disease, and follow-up care to monitor for recurrence and manage complications. Together these measures aim to reduce illness, death, and improve quality of life [1].

Cervical cancer is one of the most common gynaecological malignancies affecting women worldwide and represents a significant cause of morbidity and mortality, particularly in developing nations. It develops from the epithelial cells lining the cervix, mainly through a gradual transformation from precancerous lesions to invasive cancer, a process that typically takes several years [2]. The primary etiological factor responsible for cervical cancer is persistent infection with

high-risk strains of the human papillomavirus (HPV), particularly types 16 and 18, which together account for nearly 70% of all cases globally [3].

Globally, cervical cancer ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death among women. In 2020, there were an estimated 604,000 new cases and 342,000 deaths, highlighting the urgent need for enhanced prevention and management strategies [4]. The majority of cases occur in low- and middle-income countries where screening programs, HPV vaccination coverage, and treatment facilities remain inadequate [5]. In contrast, developed nations have observed a significant decline in incidence and mortality due to widespread implementation of organized screening programs, such as the Papanicolaou (Pap) smear and HPV testing.The pathogenesis of cervical cancer involves complex interactions between viral oncogenes and host cellular mechanisms. The viral genes E6 and E7 disrupt normal cell cycle control by inactivating tumor suppressor proteins p53 and Rb, leading to uncontrolled cellular proliferation and malignant transformation. Persistent HPV infection, combined with cofactors such as early sexual activity, multiple sexual partners, immunosuppression, smoking, and long-term oral contraceptive use, increases the risk of developing cervical neoplasi. Effective management of cervical cancer encompasses prevention, early detection, and appropriate therapeutic intervention. Primary prevention includes HPV vaccination, which has shown to be highly effective in preventing infection with high-risk HPV types and reducing precancerous lesions [6]. Secondary prevention relies on regular screening through Pap smear and HPV DNA testing to identify precancerous changes at an early and treatable stage [7]. Early-stage cervical cancer can often be treated successfully with surgery or radiotherapy, while advanced stages may require concurrent chemoradiation using agents such as cisplatin [8]. Recent advances in oncology have introduced targeted therapy and immunotherapy as promising options for recurrent or metastatic cervical cancer [9]. Bevacizumab, an angiogenesis inhibitor, has been approved as part of combination therapy to improve survival outcomes. Moreover, the inclusion of checkpoint inhibitors such as pembrolizumab has opened new avenues in the management of advanced disease [10]. The integration of these novel therapeutic approaches with established treatment protocols has led to improved survival and quality of life for many patients. Despite these advancements, the global disparity in cervical cancer outcomes persists, primarily due to inequities in healthcare access and lack of awareness [11]. The World Health Organization (WHO) has launched a global strategy aiming to eliminate cervical cancer as a public health problem through widespread HPV vaccination, comprehensive screening, and effective management of all detected cases. Achieving this goal requires coordinated public health initiatives, education, and infrastructure strengthening, particularly in resource-limited settings. Hence, understanding the management of cervical cancer from prevention to treatment is crucial for improving women's health outcomes and achieving global cancer control targets [12].

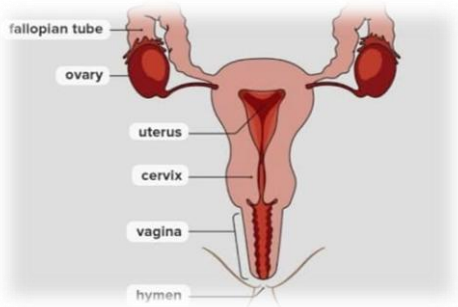

Fig 1: Image of Anatomical Structure of Female Reproductive System.

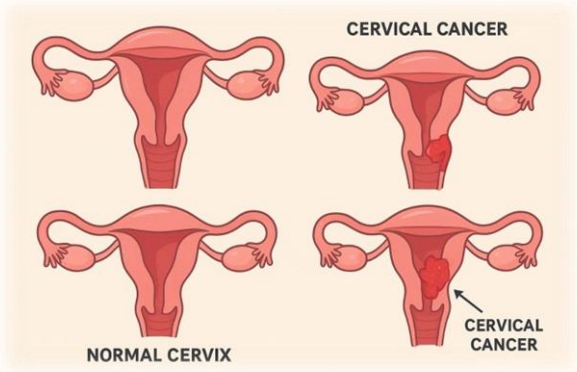

Fig 2: Image of Diagrammatic Representation of Cervical Cancer.

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HISTORY AND BACKGROUND OF MANAGEMENT OF CERVICAL CANCER

The understanding and management of cervical cancer have evolved significantly over the centuries. Early descriptions of uterine malignancies date back to ancient Egyptian and Greek medicine, but it was not until the 19th century that pathologists like Rudolf Virchow recognized cervical cancer as a distinct disease entity [13]. In the early 20th century, advances in gynecologic surgery and the introduction of radical hysterectomy by Ernst Wertheim marked a turning point in treatment [14].

A major breakthrough occurred in 1941, when Dr. George Papanicolaou developed the Pap smear test, enabling early detection of precancerous and malignant cervical lesions, which drastically reduced mortality [15]. The discovery of the human papillomavirus (HPV) as the main causative agent by Harald zur Hausen in the late 20th century further transformed prevention strategies [16]. This led to the development of HPV vaccines and targeted therapies, which now play vital roles in prevention and management [17].

Modern management integrates surgery, radiotherapy, chemotherapy, and immunotherapy based on disease stage, with an emphasis on screening and vaccination as the most effective preventive tools. Continuous global efforts focus on early detection, awareness, and equitable access to treatment to reduce the burden of cervical cancer [18].

EPIDIMOLOGY

Cervical cancer remains a significant global health concern, particularly affecting women in low- and middle-income countries. According to the World Health Organization, it is the fourth most common cancer among women worldwide, with an estimated 604,000 new cases and 342,000 deaths in 2020. The incidence and mortality rates vary widely by region, largely due to differences in screening coverage, HPV vaccination, and access to treatment [19].

NEW CASES OF CERVICAL CANCER BY STAGES

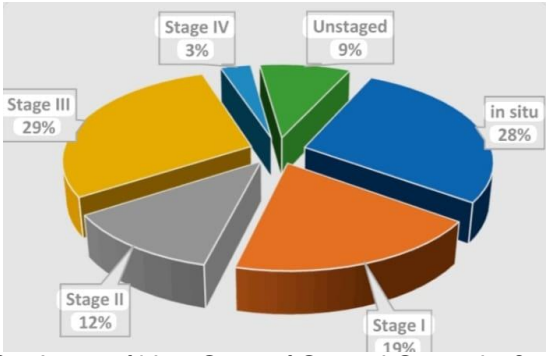

Fig 03: Image of New Cases of Cervical Cancer by Stages.

Because of systematic screening programs and extensive HPV vaccination, the incidence of cervical cancer has steadily decreased in high-income nations [20]. Sub-Saharan Africa, Southeast Asia, and Latin America, on the other hand, have the largest burden, frequently as a result of inadequate healthcare infrastructure, delayed diagnosis, and ignorance [21]. Although precancerous lesions can appear considerably earlier, the age-specific incidence peaks between the ages of 35 and 44 [22]. According to epidemiological research, immunosuppression, early sexual activity, multiple sexual partners, and chronic infection with high-risk HPV strains are important risk factors. Disease prevalence and outcomes are also influenced by socioeconomic factors, including income level and education [23]. Implementing successful preventive, screening, and management programs requires an understanding of the regional and worldwide epidemiology of cervical cancer.

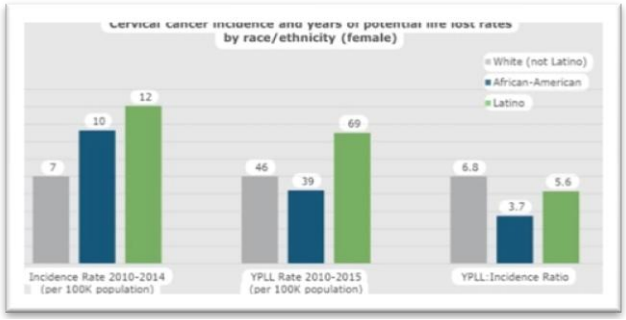

Fig 04: Image of worldwide epidemiology of cervical cancer.

SIGNS AND SYMPTOMS

Abnormal Vaginal Bleeding

The most common presenting symptom of cervical cancer is abnormal vaginal bleeding. This includes postcoital bleeding, intermenstrual bleeding, or menorrhagia. Such bleeding is often painless and may initially be intermittent, making early recognition difficult [24].

Vaginal Discharge

Patients may experience abnormal vaginal discharge, which can be watery, blood-stained, or foul-smelling. This symptom often indicates cervical epithelial disruption caused by tumor growth [25].

Pelvic and Back Pain

As the tumor enlarges and invades surrounding tissues, patients may develop pelvic pain, lower back pain, or leg discomfort. These symptoms are typically associated with more advanced disease stages [26].

Urinary and Gastrointestinal Symptoms

complaints such as dysuria, frequency, urgency, or hematuria. Tumor invasion into the bladder or rectum can lead to urinary Gastrointestinal symptoms, including constipation, rectal bleeding, and tenesmus, may also occur [27].

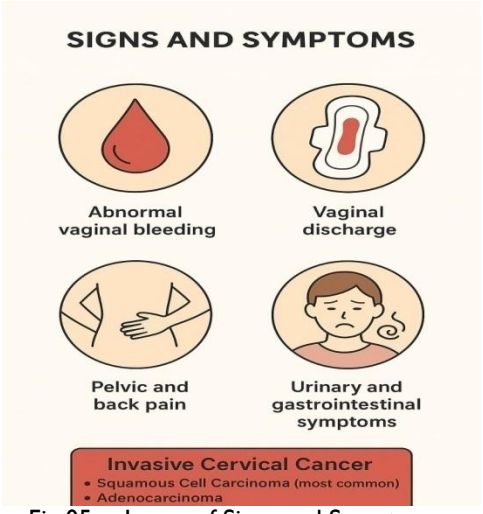

Fig 05: Image of Signs and Symptoms.

4.5. Systemic Manifestations

Advanced cervical cancer may present with systemic features such as fatigue, anemia, and weight loss, reflecting chronic blood loss and metabolic demands imposed by the malignancy (29,30). Lower limb edema may also occur due to lymphatic obstruction in some cases [28].

Early recognition of these signs and symptoms is crucial for timely diagnosis, treatment, and improved prognosis [29].

PATHOPHYSIOLOGY

The pathophysiology of cervical cancer primarily involves persistent infection with high-risk human papillomavirus (HPV) types that lead to cellular and molecular alterations in the cervical epithelium. HPV is a double-stranded DNA virus, and more than 200 genotypes have been identified, of which HPV-16 and HPV-18 are responsible for nearly 70% of cervical cancer cases worldwide [30]. The virus infects the basal cells of the squamous epithelium, typically at the transformation zone of the cervix, where squamous and columnar cells meet-a region highly susceptible to viral entry [31]. Following infection, the viral genome integrates into the host DNA, resulting in the overexpression of two key

oncogenes, E6 and E7, which play a crucial role in carcinogenesis [31]. The E6 protein binds to the tumor suppressor protein p53, resulting in the loss of apoptotic regulation and its degradation. In a similar vein, the retinoblastoma (Rb) protein is rendered inactive by the E7 protein, leading to unchecked cell cycle progression and genomic instability [32]. Together, these molecular processes lead to aberrant cell division, dysplasia, and eventually the malignant transformation of cervical epithelial cells. Infection persistence and the development of invasive carcinoma and high-grade squamous intraepithelial lesions (HSIL) are further accelerated by persistent inflammation and immune evasion [33]. The course of the disease is also altered by host variables as immunosuppression, co-infections, hormonal effects, and genetic predisposition. The transition from preinvasive to invasive cervical cancer is characterized by the accumulation of genetic and epigenetic changes over time, which leads to the invasion of malignant cells through the basement membrane into adjacent tissues [34].

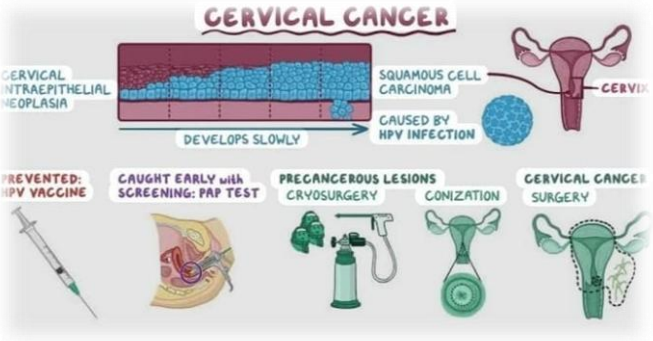

Fig 6: Image of cervical cancer.

DIAGNOSIS OF CERVICAL CANCER

Methods of screening:

The first step in diagnosing cervical cancer is usually screening for malignant or precancerous alterations in the cervix. The most used screening technique is the Papanicolaou (Pap) smear test. Early intervention before invasive cancer develops is made possible by its assistance in identifying aberrant epithelial cells [35]. Furthermore, human papillomavirus (HPV) DNA testing is essential for identifying high-risk viral strains like HPV-16 and HPV-18, which cause most occurrences of cervical cancer [36].

Dignostic Assessment:

Colposcopy is used to inspect the cervix under magnification and find suspicious lesions if screening results show abnormalities. Biopsy samples are taken throughout this process for histological analysis, which verifies malignancy and establishes the lesion's grade [37].

Staging and Imaging

Imaging methods such as Magnetic Resonance Imaging (MRI), Computed Tomography (CT), and Positron Emission Tomography (PET) scans are used to assess the degree and stage of cervical cancer, which helps with treatment planning [38].

The Value of Early Identification

Survival rates are greatly enhanced by early diagnosis. HPV testing, routine screening and prompt follow-up of abnormal findings continue to be essential tactics for lowering the death rate from cervical cancer [39].

Diagnosis

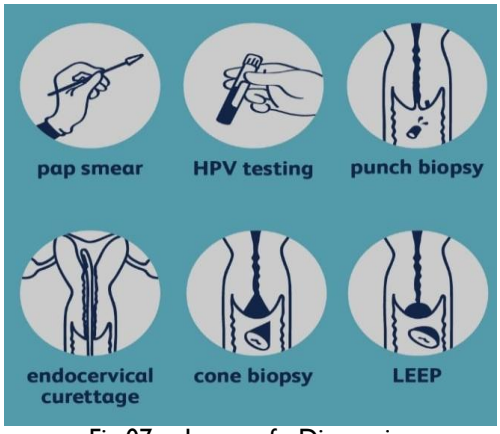

Fig 07: Image of Diagnosis.

TREATMENT OF CERVICAL CANCER

Cervical cancer in its early stages (FIGO I–IIA)

The cornerstone of treatment for early-stage cervical cancer is surgery. Women who do not want to preserve their fertility frequently undergo radical hysterectomy with pelvic lymph node dissection [40]. Radical trachelectomy with lymph node evaluation is an option for younger women who want to maintain their fertility. Patients with high-risk pathological characteristics, such as parametrial invasion, positive margins, or lymph node involvement, may benefit from adjuvant radiotherapy or chemoradiation.

Cervical cancer that has progressed locally (FIGO IIB–IVA)

For locally advanced illness, concurrent chemoradiation is the recommended course of treatment [41]. To increase local control and overall survival, cisplatin-based chemotherapy is used in conjunction with intracavitary brachytherapy and external beam radiation [42, 43].

Advanced radiotherapy techniques, such as intensity-modulated radiotherapy (IMRT), are employed to minimize toxicity to surrounding organs while delivering an effective dose to the tumor.

Metastatic or Recurrent Cervical Cancer.

The main treatment for recurrent or metastatic disease is systemic chemotherapy, which frequently uses topotecan, paclitaxel, or cisplatin [44]. When used with chemotherapy, the anti-angiogenic monoclonal antibody bevacizumab has been shown to improve survival results. Patients with PD-L1 positive malignancies should get immunotherapy with pembrolizumab, a PD-1 inhibitor that produces long-lasting effects in advanced illness [45].

Assistance

Maintaining quality of life requires supportive care, which includes pain management, dietary support, and treatment of side effects associated to therapy. Optimizing survival

and clinical outcomes requires a multidisciplinary strategy that is adapted to the patient's demands, tumor characteristics, and disease stage.

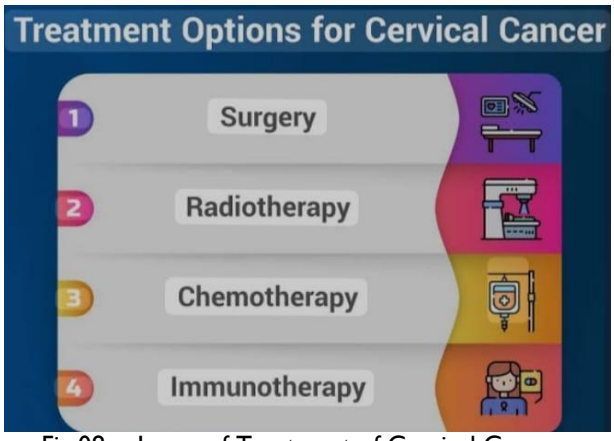

Fig 08: Image of Treatment of Cervical Cancer.

DRUGS USED IN MANAGEMENT OF CERVICAL CANCER.

Table 01: Drugs Used In Management of Cervical Cancer.

SL.NO	DRUG NAME	CLASS	MECHANISM OF ACTION	CLINICAL USE
1.	Cisplatin	Platinum based chemo	Forms DNA crosslinks - inhibits DNA replicatioinand transccriptiion-induces apoptosis	First line chemotheraphy,concurrent with radiotheraphy
2.	Carboplatin	Platinum based chemo	DNA crosslinking-apoptosis	Alternative to cispaltin in advanced or metastatis disease
3.	Paclitaxel	Taxane	Stabilizes microtubules-inhibits mitosis-apoptosis	Combined with cisplatin for advanced/metastatic disease
4.	Topotecan	Topoisomerase inhibitor	Inhibits topoisomerase I-DNA damage -cell death	Second line chemotheraphy for recurrent/metastatic disease
5.	Bevacizumab	Monoclonal antibody	VEGF inhibitor-inhibits angiogenesis	Used in combinatin wiith chemotheraphyfor advanced cervical cancer
6.	Pembrolizumab	Immune checkpoint inhibitor	PD-1 inhibitor-enhances T-cell mediated anti tumor response	For a recurrent or metastaticPD-L1positive cervical cancer
7.	5-Fluorouracil(5-FU)	Antimetabolite	Inhibits thymidylate synthase-blocks DNA synthesis	Often combined with cisplatin for chemoradiaton protocols.

ADVERSE EFFECTS OF CERVICAL CANCER TREATMENT

Treatment of cervical cancer, including surgery, radiotherapy, chemotherapy, and immunotherapy, can result in various adverse effects. Surgical interventions such as radical hysterectomy may cause bladder dysfunction, urinary incontinence, sexual dysfunction, and lymphatic complications [46,47]. Radiotherapy, particularly pelvic irradiation, can lead to acute gastrointestinal symptoms like nausea, diarrhea, and proctitis, as well as late effects including bowel obstruction, fibrosis, and radiation cystitis [47,48]. Cisplatin-based chemotherapy may cause nephrotoxicity, neurotoxicity, myelosuppression, nausea, and vomiting [49]. Combination

regimens with paclitaxel can additionally induce neuropathy, alopecia, and hypersensitivity reactions.Targeted therapy such as bevacizumab is associated with hypertension, proteinuria, and increased risk of thromboembolic events. Immune checkpoint inhibitors like pembrolizumab may lead to immune-related adverse events including colitis, pneumonitis, hepatitis, and endocrinopathies [50]. Awareness and management of these toxicities are crucial for maintaining treatment efficacy and patient quality of life.

RISK FACTORS FOR CERVICAL CANCER

Human Papillomavirus (HPV) Infection

Persistent infection with high-risk HPV types, especially HPV-16 and HPV-18, is the most significant risk factor for cervical cancer [51,52]. Viral oncogenes E6 and E7 disrupt tumor suppressor proteins, promoting malignant transformation.

Sexual and Reproductive Factors

Early onset of sexual activity, multiple sexual partners, and multiparity increase the risk of cervical cancer by enhancing exposure to HPV infection [52,53].

Immunosuppression

Women with immunosuppressive conditions, such as HIV infection or post-transplant immunosuppression, have a higher risk due to impaired clearance of HPV [53,54].

Lifestyle and Environmental Factors

Smoking, long-term oral contraceptive use, and poor socioeconomic status are associated with increased risk, possibly by promoting viral persistence and cervical epithelial changes [54, 55].

Genetic Susceptibility

Certain genetic polymorphisms affecting immune response may predispose individuals to persistent HPV infection and cervical carcinogenesis [55].

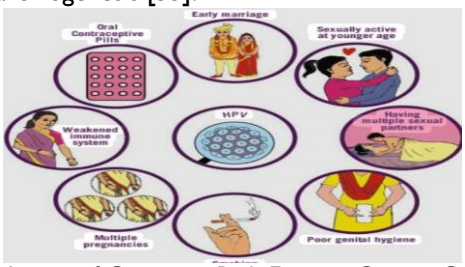

Fig 09: Image of Common Risk Factors Causes Cervical Cancer.

PREVENTION OF CERVICAL CANCER:

Primary, secondary, and tertiary measures are used to prevent cervical cancer. HPV vaccination, which successfully guards against high-risk HPV strains that cause most cervical malignancies, is the mainstay of primary prevention [56, 57]. Regular screening with Pap smears, HPV DNA testing, or visual inspection with acetic acid (VIA) to identify precancerous lesions early are examples of secondary prevention [58, 59]. Risk is also decreased by lifestyle changes such quitting smoking and using safe sexual practices [59]. Through follow-up and early intervention in treated instances, tertiary prevention seeks to avoid recurrence [60]. Reducing the incidence of cervical cancer worldwide requires a mix of screening, immunization, and health education.

Fig 10: Image of Prevention of Cervical Cancer.

DRUGS APPROVED TO PREVENT CERVICAL CANCER

The prevention of cervical cancer primarily relies on prophylactic vaccines that protect against infection with high-risk human papillomavirus (HPV) types responsible for the majority of cervical cancer cases [61]. These vaccines contain virus-like particles (VLPs) derived from the HPV L1 protein, which induce strong immune responses without containing viral DNA, making them non-infectious and highly safe [62].

Bivalent Vaccine (Cervarix®)

Cervarix®, developed by GlaxoSmithKline, targets HPV types 16 and 18, which cause approximately 70% of cervical cancers [63]. It utilizes the AS04 adjuvant system to enhance immunogenicity and has shown long-term protection lasting over a decade [64].

Quadrivalent Vaccine (Gardasil®)

Gardasil®, produced by Merck, offers protection against HPV types 6, 11, 16, and 18. In addition to preventing cervical cancer, it protects against genital warts caused by HPV types 6 and 11 [65]. Clinical trials have demonstrated over 95% efficacy in preventing high-grade cervical lesions among vaccinated individuals [65].

Nonavalent Vaccine (Gardasil 9®)

Gardasil 9® extends coverage to nine HPV types (6, 11, 16, 18, 31, 33, 45, 52, and 58), providing broader protection against nearly 90% of cervical cancer-causing strains [66]. It is approved globally and recommended for both males and females from adolescence through young adulthood. These vaccines represent a landmark achievement in cancer prevention, significantly reducing the incidence of HPV-related precancerous lesions and cervical cancer worldwide.

Fig 11: Image of Nonavalent Vaccine.

FUTURE THERAPIES AND TRENDS IN CERVICAL CANCER

Immunotherapy

PD-1 and PD-L1 inhibitors are examples of immune checkpoint inhibitors that are showing promise as therapies for metastatic or recurrent cervical cancer. In certain patients, they provide long-lasting responses by strengthening T-cell-mediated anti-tumor responses [67].

Targeted Treatment

In order to improve survival results, novel targeted medicines, such as PARP inhibitors and anti-angiogenic medications, are being researched to disrupt particular molecular pathways implicated in tumor growth and metastasis [68].

Therapeutic Immunizations

Therapeutic HPV vaccines, which have shown potential in early clinical studies, seek to boost immune responses against already-existing HPV-infected or altered cells, in contrast to preventive HPV vaccinations [69].

Genomic Approaches and Personalized Medicine.

Genomic profiling developments enable tailored treatment plans based on tumor molecular features, maximizing therapeutic efficacy while reducing toxicity [64, 65, 67, 69, 70]. Ongoing research in these areas represents a significant shift toward precision oncology, potentially improving survival and quality of life for cervical cancer patients.

CONCLUSION

Cervical cancer remains a significant public health challenge worldwide, particularly in low- and middle-income countries where screening and HPV vaccination coverage are limited. Persistent infection with high-risk HPV types is the primary etiological factor, with additional contributions from immunosuppression, reproductive behaviours, lifestyle, and genetic susceptibility. Early detection through screening programs and timely intervention significantly improves prognosis and survival outcomes Current management strategies include surgery, radiotherapy, chemoradiation, targeted therapy, and immunotherapy, with treatment tailored to disease stage and patient-specific factors. Advances in HPV vaccination, precision medicine, and novel therapeutic approaches, including immunotherapy and therapeutic vaccines, hold promise for reducing disease burden and improving patient quality of life. Comprehensive prevention, early diagnosis, multidisciplinary treatment, and ongoing research are essential to achieve the global goal of cervical cancer elimination and to enhance clinical outcomes for affected women.

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Nil

CONFLICT OF INTEREST

Authors are declared that no conflict of interest

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INFORM CONSENT AND ETHICAL CONSIDERATIONS

Not Applicable

REFERENCES

1. World Health Organization (WHO). Cervical Cancer: Prevention and Control. Geneva: World Health Organization; 2023. Available from: https://www.who.int/health-topics/cervical-cancer
2. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Cervical Cancer. Version 1.2025. Available at: https://www.nccn.org
3. Arbyn M, Weiderpass E, Bruni L, de Sanjosé S, Saraiya M, Ferlay J, Bray F. Estimates of incidence and mortality of cervical cancer in 2020: A worldwide analysis. The Lancet Global Health. 2021;9(2):e191–e203. https://doi.org/10.1016/S2214-109X(20)30482-6
4. Cohen PA, Jhingran A, Oaknin A, Denny L.Cervical cancer.The Lancet. 2019;393(10167):169–182. https://doi.org/10.1016/S0140-6736(18)32470-X
5. Tewari KS, Monk BJ.Management of recurrent cervical cancer.Gynecologic Oncology. 2019;152(3):505–517. https://doi.org/10.1016/j.ygyno.2018.12.025
6. National Cancer Institute (NCI).Cervical Cancer Treatment (PDQ®)–Health Professional Version. Updated 2024. Available from: https://www.cancer.gov/types/cervical/hp
7. Tjalma WA, Kim E, Van Dam PA.Prevention and management of cervical cancer: New advances and future perspectives.International Journal of Gynecology & Obstetrics. 2023;162(1):1–10. https://doi.org/10.1002/ijgo.14629
8. Centers for Disease Control and Prevention (CDC).Human Papillomavirus (HPV)Vaccination: What Everyone Should Know. Updated 2024. Available at: https://www.cdc.gov/hpv/parents/vaccine.html
9. Doorbar J, Egawa N, Griffin H, Kranjec C, Murakami I. Human papillomavirus molecular biology and disease association. Rev Med Virol. 2015;25(S1):2–23. https://doi.org/10.1002/rmv.1822
10. Bhatla N, Singhal S. Primary HPV screening for cervical cancer. Best Pract Res Clin Obstet Gynaecol. 2020;65:98–108. https://doi.org/10.1016/j.bpobgyn.2020.02.004
11. Crosbie EJ, Einstein MH, Franceschi S, Kitchener HC. Human papillomavirus and cervical cancer. Lancet. 2013;382(9895):889–899. https://doi.org/10.1016/S0140-6736(13)60022-7
12. Moody CA, Laimins LA. Human papillomavirus oncoproteins: Pathways to transformation. Nat Rev Cancer. 2010;10(8):550–560. https://doi.org/10.1038/nrc2886

13. Stanley MA. Epithelial cell responses to infection with human papillomavirus. Clin Microbiol Rev. 2012;25(2):215–222. https://doi.org/10.1128/CMR.05028-11
14. zur Hausen H. Papillomaviruses and cancer: From basic studies to clinical application. Nat Rev Cancer. 2002;2(5):342–350. https://doi.org/10.1038/nrc798
15. Wentzensen N, Schiffman M, Palmer T, Arbyn M. Triage of HPV positive women in cervical cancer screening. J Clin Virol. 2016;76(Suppl 1):S49–S55. https://doi.org/10.1016/j.jcv.2015.11.015
16. World Health Organization. Cervical Cancer: Key Facts. Geneva: WHO; 2023. https://www.who.int/news-room/fact-sheets/detail/cervical-cancer
17. Bruni L, Serrano B, Roura E, et al. HPV vaccination introduction worldwide and cervical cancer burden. Vaccine. 2021;39(2):210–220. https://doi.org/10.1016/j.vaccine.2020.11.027
18. Arbyn M, Weiderpass E, Bruni L, et al. Estimates of incidence and mortality worldwide. Lancet Glob Health. 2021;9(2):e191–e203. https://doi.org/10.1016/S2214-109X(20)30482-6
19. Garland SM, Kjaer SK, Muñoz N, et al. Impact of HPV vaccination on cervical cancer incidence. Lancet. 2016;388(10047):1647–1654. https://doi.org/10.1016/S0140-6736(16)31323-7
20. Denny L. Cervical cancer in low-resource countries. Best Pract Res Clin Obstet Gynaecol. 2012;26(2):179–189. https://doi.org/10.1016/j.bpobgyn.2011.08.004
21. Ferlay J, Colombet M, Soerjomataram I, et al. Global cancer statistics 2020. Int J Cancer. 2021;149:778–789. https://doi.org/10.1002/ijc.33588
22. Plummer M, de Martel C, Vignat J, et al. Global burden of HPV and cervical cancer. Int J Cancer. 2016;138(12):2826–2836. https://doi.org/10.1002/ijc.29911
23. Brisson M, Kim JJ, Canfell K, et al. Impact of vaccination and screening on cervical cancer. Prev Med. 2020;139:106193. https://doi.org/10.1016/j.ypmed.2020.106193
24. National Cancer Institute. Cervical Cancer Symptoms. Updated 2024. https://www.cancer.gov/types/cervical/patient/cervical-treatment-pdq
25. Denny L. Cervical cancer: Clinical presentation and diagnosis. Best Pract Res Clin Obstet Gynaecol. 2012;26(2):189–197. https://doi.org/10.1016/j.bpobgyn.2011.09.001
26. Quinn MA, Benedet JL, Odicino F, et al. FIGO 2018 staging for cervical cancer. Int J Gynaecol Obstet. 2019;145:129–135. https://doi.org/10.1002/ijgo.12749
27. Bhatla N, Singhal S. Clinical features of invasive cervical cancer. Indian J Med Res. 2017;145(4):467–474. https://doi.org/10.4103/ijmr.IJMR_1028_17
28. Tjalma WA. Clinical manifestations of advanced cervical cancer. Oncol Lett. 2014;8(1):3–10. https://doi.org/10.3892/ol.2014.2165
29. Crosbie EJ, Einstein MH, Franceschi S, Kitchener HC. Human papillomavirus and cervical cancer. Lancet. 2013;382(9895):889–899. https://doi.org/10.1016/S0140-6736(13)60022-7
30. Cohen PA, Jhingran A, Oaknin A, Denny L. Cervical cancer. Lancet. 2019;393(10167):169–182. https://doi.org/10.1016/S0140-6736(18)32470-X
31. Tewari KS, Sill MW, Long HJ 3rd, et al. Improved survival with cisplatin-based chemoradiation in cervical cancer. N Engl J Med. 2003;348:1045–1053. https://doi.org/10.1056/NEJMoa021761
32. Monk BJ, Tewari KS, Koh WJ. Management of advanced cervical cancer. Semin Oncol. 2008;35(2):181–198. https://doi.org/10.1053/j.seminoncol.2008.03.002
33. Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatin and paclitaxel in cervical cancer therapy. J Clin Oncol. 1999;17:1339–1348. https://doi.org/10.1200/JCO.1999.17.4.1339
34. Moore DH, Blessing JA, McQuellon RP, et al. Topotecan in recurrent cervical cancer. J Clin Oncol. 2004;22:3113–3119. https://doi.org/10.1200/JCO.2004.01.159
35. Tewari KS, Sill MW, Long HJ 3rd, et al. Bevacizumab for advanced cervical cancer. N Engl J Med. 2014;370:734–743. https://doi.org/10.1056/NEJMoa1309748
36. Colombo N, Dubot C, Lorusso D, et al. Pembrolizumab in recurrent or metastatic cervical cancer. Gynecol Oncol. 2021;161(1):195–203. https://doi.org/10.1016/j.ygyno.2020.11.014
37. Keys HM, Bundy BN, Stehman FB, et al. 5-Fluorouracil and cisplatin chemoradiation in cervical cancer. J Clin Oncol. 1999;17:1339–1348. https://doi.org/10.1200/JCO.1999.17.4.1339
38. Tewari KS, Sill MW, Long HJ 3rd, et al. Improved survival with cisplatin-based chemoradiation in cervical cancer. N Engl J Med. 2003;348:1045–1053. https://doi.org/10.1056/NEJMoa021761
39. Landoni F, Maneo A, Colombo A, et al. Randomized study of radical surgery vs radiotherapy in early-stage cervical cancer. Lancet. 1997;350:535–540. https://doi.org/10.1016/S0140-6736(97)04239-2
40. Smith HO, Owens CL, Goff BA. Fertility-sparing surgery in early-stage cervical cancer. Obstet Gynecol. 2008;112:178–186. https://doi.org/10.1097/AOG.0b013e3181788df3
41. Peters WA 3rd, Liu PY, Barrett RJ 2nd, et al. Concurrent chemotherapy and pelvic radiation therapy in high-risk early-stage cervical cancer. N Engl J Med. 2000;340:1137–1143. https://doi.org/10.1056/NEJM200004203401402
42. Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatin-based radiotherapy in locally advanced cervical

cancer. N Engl J Med. 1999;340:1144–1153. https://doi.org/10.1056/NEJM199904223401403
43. Klopp AH, Yeung AR, Deshmukh S. Advanced radiotherapy techniques in cervical cancer. Int J Radiat Oncol Biol Phys. 2014;88:1–12. https://doi.org/10.1016/j.ijrobp.2013.11.013
44. Tewari KS, Sill MW, Long HJ 3rd, et al. Bevacizumab in advanced cervical cancer. N Engl J Med. 2014;370:734–743. https://doi.org/10.1056/NEJMoa1309748
45. Colombo N, Dubot C, Lorusso D, et al. Pembrolizumab in recurrent or metastatic cervical cancer. Gynecol Oncol. 2021;161(1):195–203. https://doi.org/10.1016/j.ygyno.2020.11.014
46. Bhatla N, Singhal S. Surgical complications in cervical cancer management. Indian J Med Res. 2017;145(4):475–483. https://doi.org/10.4103/ijmr.IJMR_1029_17
47. Viswanathan AN, Thomadsen B. Adverse effects of radiotherapy in cervical cancer. Semin Radiat Oncol. 2012;22:243–251. https://doi.org/10.1016/j.semradonc.2012.01.002
48. Small W Jr, Bacon MA, Bajaj A, et al. Radiation therapy for cervical cancer: Side effects and management. J Clin Oncol. 2017;35:203–218. https://doi.org/10.1200/JCO.2016.70.6353
49. Moore DH, Blessing JA, McQuellon RP, et al. Chemotherapy toxicities in cervical cancer. J Clin Oncol. 2004;22:3113–3119. https://doi.org/10.1200/JCO.2004.01.159
50. Colombo N, Dubot C, Lorusso D, et al. Immune and targeted therapy-related adverse effects in cervical cancer. Gynecol Oncol. 2021;161(1):195–203. https://doi.org/10.1016/j.ygyno.2020.11.014
51. Bosch FX, Lorincz A, Muñoz N, et al. The causal relation between HPV and cervical cancer. J Clin Pathol. 2002;55:244–265. https://doi.org/10.1136/jcp.55.4.244
52. Bhatla N, Singhal S. HPV and cervical cancer risk factors. Indian J Med Res. 2017;145(4):467–474. https://doi.org/10.4103/ijmr.IJMR_1028_17
53. zur Hausen H. Papillomaviruses and cancer: Molecular mechanisms. Nat Rev Cancer. 2002;2:342–350. https://doi.org/10.1038/nrc798
54. Plummer M, de Martel C, Vignat J, et al. Global burden and risk factors of cervical cancer. Int J Cancer. 2016;138:2826–2836. https://doi.org/10.1002/ijc.29911
55. Wentzensen N, Schiffman M, Palmer T, Arbyn M. Genetic susceptibility and cervical cancer. J Clin Virol. 2016;76(Suppl 1):S49–S55. https://doi.org/10.1016/j.jcv.2015.11.015
56. World Health Organization. Cervical Cancer Prevention and Control. Geneva: WHO; 2023. https://www.who.int/health-topics/cervical-cancer
57. Garland SM, Kjaer SK, Muñoz N, et al. Impact of HPV vaccination on cervical cancer. Lancet. 2016;388:1647–1654. https://doi.org/10.1016/S0140-6736(16)31323-7
58. Arbyn M, Weiderpass E, Bruni L, et al. Screening for cervical cancer worldwide. Lancet Glob Health. 2021;9:e191–e203. https://doi.org/10.1016/S2214-109X(20)30482-6
59. Plummer M, de Martel C, Vignat J, et al. Prevention strategies and lifestyle factors. Int J Cancer. 2016;138:2826–2836. https://doi.org/10.1002/ijc.29911
60. Denny L. Tertiary prevention and follow-up in cervical cancer. Best Pract Res Clin Obstet Gynaecol. 2012;26:199–210. https://doi.org/10.1016/j.bpobgyn.2011.08.004
61. Colombo N, Dubot C, Lorusso D, et al. Immunotherapy in cervical cancer. Gynecol Oncol. 2021;161:195–203. https://doi.org/10.1016/j.ygyno.2020.11.014
62. Tewari KS, Sill MW, Long HJ 3rd, et al. Targeted therapies in advanced cervical cancer. N Engl J Med. 2014;370:734–743. https://doi.org/10.1056/NEJMoa1309748
63. Trimble CL, Frazer IH. Therapeutic HPV vaccines. Vaccine. 2009;27(Suppl 2):B108–B115. https://doi.org/10.1016/j.vaccine.2009.08.068
64. Foulkes WD, Smith IE, Reis-Filho JS. Personalized medicine in cervical cancer. N Engl J Med. 2010;363:1938–1947. https://doi.org/10.1056/NEJMra1001682
65. Ojesina AI, Lichtenstein L, Freeman SS, et al. Genomic landscape of cervical cancer and precision therapy. Nat Genet. 2014;46:1071–1076. https://doi.org/10.1038/ng.3046
66. World Health Organization. Global Strategy to Accelerate the Elimination of Cervical Cancer. Geneva: WHO; 2020. https://www.who.int/publications/i/item/9789240014107
67. Arbyn M, Weiderpass E, Bruni L, et al. Estimates of incidence and mortality worldwide. Lancet Glob Health. 2021;9:e191–e203. https://doi.org/10.1016/S2214-109X(20)30482-6
68. Bosch FX, Lorincz A, Muñoz N, et al. The causal relation between HPV and cervical cancer. J Clin Pathol. 2002;55:244–265. https://doi.org/10.1136/jcp.55.4.244
69. Tewari KS, Sill MW, Long HJ 3rd, et al. Bevacizumab in advanced cervical cancer. N Engl J Med. 2014;370:734–743. https://doi.org/10.1056/NEJMoa1309748
70. Colombo N, Dubot C, Lorusso D, et al. Future trends and therapies in cervical cancer. Gynecol Oncol. 2021;161:195–203. https://doi.org/10.1016/j.ygyno.2020.11.014
71. World Health Organization. Human papillomavirus vaccines: WHO position paper. Wkly Epidemiol Rec. 2022;97(24):289–310.
72. Harper DM, Franco EL, Wheeler C, et al. Efficacy of a bivalent L1 virus-like particle vaccine in prevention of HPV infection and cervical cancer. N Engl J Med.

2004;350:523–532. https://doi.org/10.1056/NEJMoa032191
73. Paavonen J, Jenkins D, Bosch FX, et al. Efficacy of a prophylactic HPV vaccine against cervical infection and neoplasia. Lancet. 2007;369:2161–2170. https://doi.org/10.1016/S0140-6736(07)60946-5
74. Villa LL, Costa RL, Petta CA, et al. High sustained efficacy of a prophylactic quadrivalent HPV vaccine. Br J Cancer. 2006;95:1459–1466. https://doi.org/10.1038/sj.bjc.6603469
75. Joura EA, Giuliano AR, Iversen OE, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia. N Engl J Med. 2015;372:711–723. https://doi.org/10.1056/NEJMoa1405044
76. World Health Organization. Comprehensive cervical cancer control: a guide to essential practice, 3rd ed. WHO, 2023.
77. Papanicolaou GN. A new procedure for staining vaginal smears. Science. 1942;95(2469):438–439.
78. Schiffman M, Castle PE, Jeronimo J, et al. Human papillomavirus and cervical cancer. Lancet. 2007;370(9590):890–907.
79. Massad LS, Einstein MH, Huh WK, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests. J Low Genit Tract Dis. 2013;17(5 Suppl 1):S1–S27.
80. Bhatla N, Aoki D, Sharma DN, et al. FIGO cancer report 2021: cervical cancer staging and diagnosis. Int J Gynecol Obstet. 2021;155(1):77–90.