IJBPAS, March, 2026, 15(3): 1139-1150

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

TREATMENTS FOR CERVICAL CANCER: PRESENT DIFFICULTIES AND PROSPECTS

VASANTHA G[1*], PANJA RATNASRI SAI DP[2], SAGARIKA Y[2] AND PRIYANKA D[2]

1: Associate Professor, HoD, Dept of Pharmacology, Vignan Institute of Pharmaceutical Technology, (Autonomous), (Affiliated to JNTUGV) Vishakapatnam, Andhra Pradesh, India, 530049.

2: IVB.Pharmacy, Vignan Institute of Pharmaceutical Technology, (Autonomous), (Affiliated to JNTUGV) Vishakapatnam, Andhra Pradesh, India, 530049

*Corresponding Author: Dr. Galanki Vasantha: E Mail: drvasanthaniper@gmail.com

Received 20th Oct. 2024; Revised 15th Dec. 2024; Accepted 15th Feb. 2025; Available online 1st March 2026

https://doi.org/10.31032/IJBPAS/2026/15.3.9925

ABSTRACT

Almost 300,000 women die from cervical cancer each year, making it the fourth most frequent cancer in the world among women. The human papillomavirus high-risk subtypes that cause cervical cancer are the primary cause of the disease. Together with host factors, the E5, E6, and E7 viral proto-oncogene start and maintain the maligant phenotype. In low- and middle-income nations, however, the disease is fatal for women because of their limited resources, which frequently result in advanced and incurable sickness. Radiation therapy, chemotherapy, and/or surgery are available as treatments, either separately or in combination. This review outlines the causes and symptoms of cervical cancer and goes into detail about the benefits and drawbacks of the current cervical cancer therapies. The future of cervical cancer treatment is then covered, including immunotherapies, targeted medicines, combination therapies, and genetic treatment options.

KEY FACTS:

According to estimates, cervical cancer will account for 350 000 deaths and 660 000 new cases in 2022, making it the fourth most frequent malignancy among women globally.

• Low- and middle-income countries see higher rates of cervical cancer incidence and

mortality. This demonstrates large discrepancies caused by a lack of access to national HPV vaccine, cervical examination, and therapy programs, as well as socioeconomic considerations.

• Consistent infection with the human papillomavirus (HPV) leads to cervical cancer. Women with HIV are six times more likely to get cervical cancer than women without HIV.

• Prophylactic HPV vaccine, as well as pre-cancer screening and therapy, are cost-effective strategies for preventing cervical cancer.

•Women living with HIV are six times more likely to get cervical cancer than women who do not have HIV.

Early detection can lead to cures for cervical cancer.

OVERVIEW:

Cervical cancer is the fourth most frequent malignancy in women worldwide; in 2022, there will be over 660 000 new cases. Approximately 94% of the 350 000 cervical cancer-related fatalities that year happened in low- and middle-income nations. South-East Asia, Central America, and sub-Saharan Africa (SSA) have the greatest incidence and fatality rates of cervical cancer. Variations in the incidence of cervical cancer among regions are associated with disparities in the availability of immunisation, screening, and treatment programs; risk factors such as the prevalence of HIV; and social and economic factors like gender stereotypes, sexism, and poverty. Compared to the general population, women living with HIV are six times more likely to acquire cervical cancer, and an estimated 5% of all incidences of cervical cancer are related to HIV **[1]**. Because younger women are disproportionately affected by cervical cancer, 20% of children whose mothers die from cancer do so as a result of cervical cancer **[2]**.

INTRODUCTION:

Representing 20% of the global cancer burden, cervical cancer is the second most common malignancy among women globally **[1]**. According to Estimation, there will be an 85% rise in new cases of cervical cancer in less developed countries by 2026 **[2]**. HPV, or high-risk human papillomavirus, is the single most significant etiological cause of cervical cancer **[3]**. Many things can lead to cervical cancer, such as HPV, smoking, having multiple sexual partners, using birth control tablets for an extended period of time, and starting sexual activity young **[4]**. A group of viruses that comprise eight double strands of DNA have been linked to a variety of illnesses that impact epithelial cells **[5]**. Indeed, up to 99.7% of cases of cervical cancer are caused by chronic infection with high-risk HPV types **[6, 7]**. The strategy's

three primary objectives are to vaccinate 90% of girls before the age of 15, screen 70% of women between the ages of 35 and 45 using an HPV-based test, and ensure that 90% of women who have abnormal cells on their cervix surface receive appropriate care from trained professionals **[6]**.

INITIATION AND PROGRESSION OF CERVICAL CANCER:

The uterus's cervix, which connects to the cervical cancer starts to spread through the endocervical canal **(Figure 1A)** in the vagina **[7]**. The ectocervix and endocervix are two distinct sections of the cervix. Simple columnar epithelial cells cover the endocervix, while stratified squamous epithelial cells cover the ectocervix. Where these sections converge is known as the "transformation zone," where columnar lined epithelium is replaced by metaplastic epithelium. Since it is the main location of premalignant changes such persistent HPV infection **(Figure 1A)**, this zone is the most likely place for cervical cancer to develop **[7]**. Two primary histological subtypes of cervical cancer are adenocarcinoma and squamous cell carcinoma (SCC) **(Figure 1B)**.

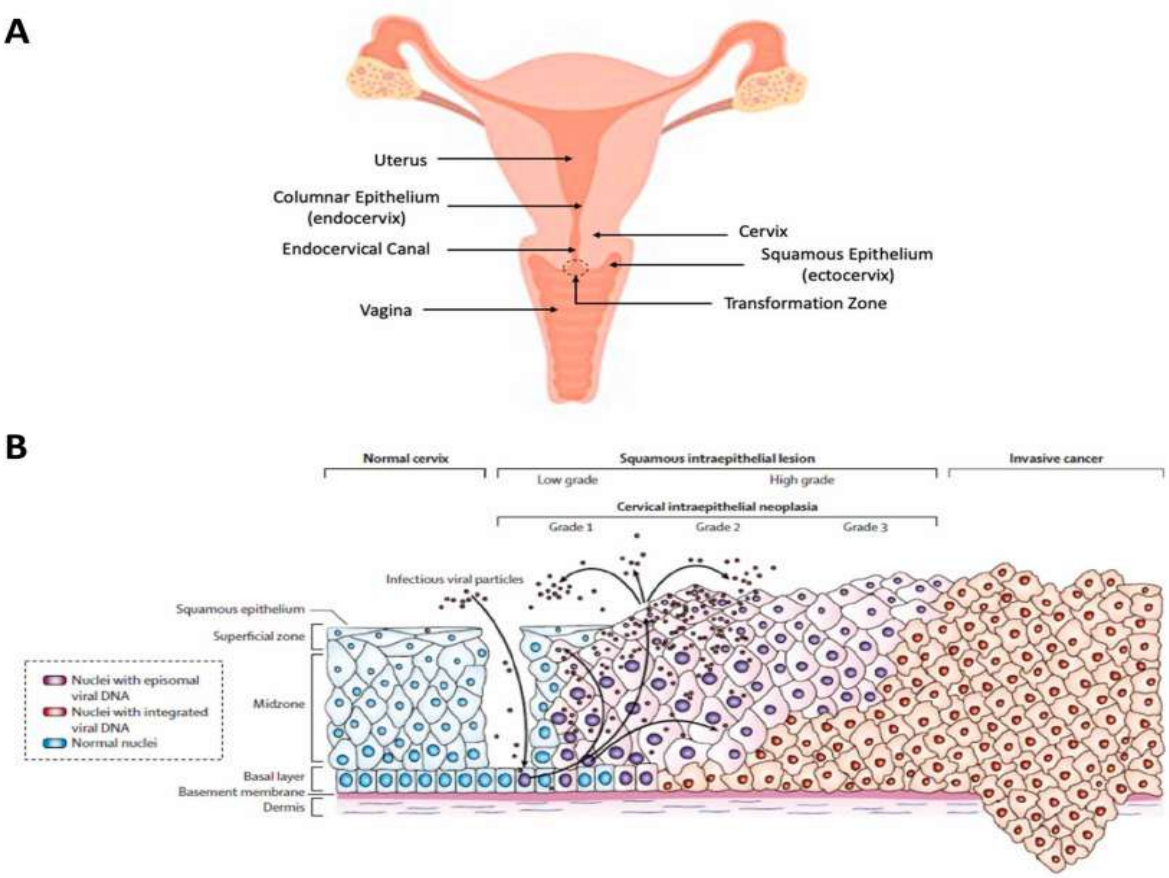


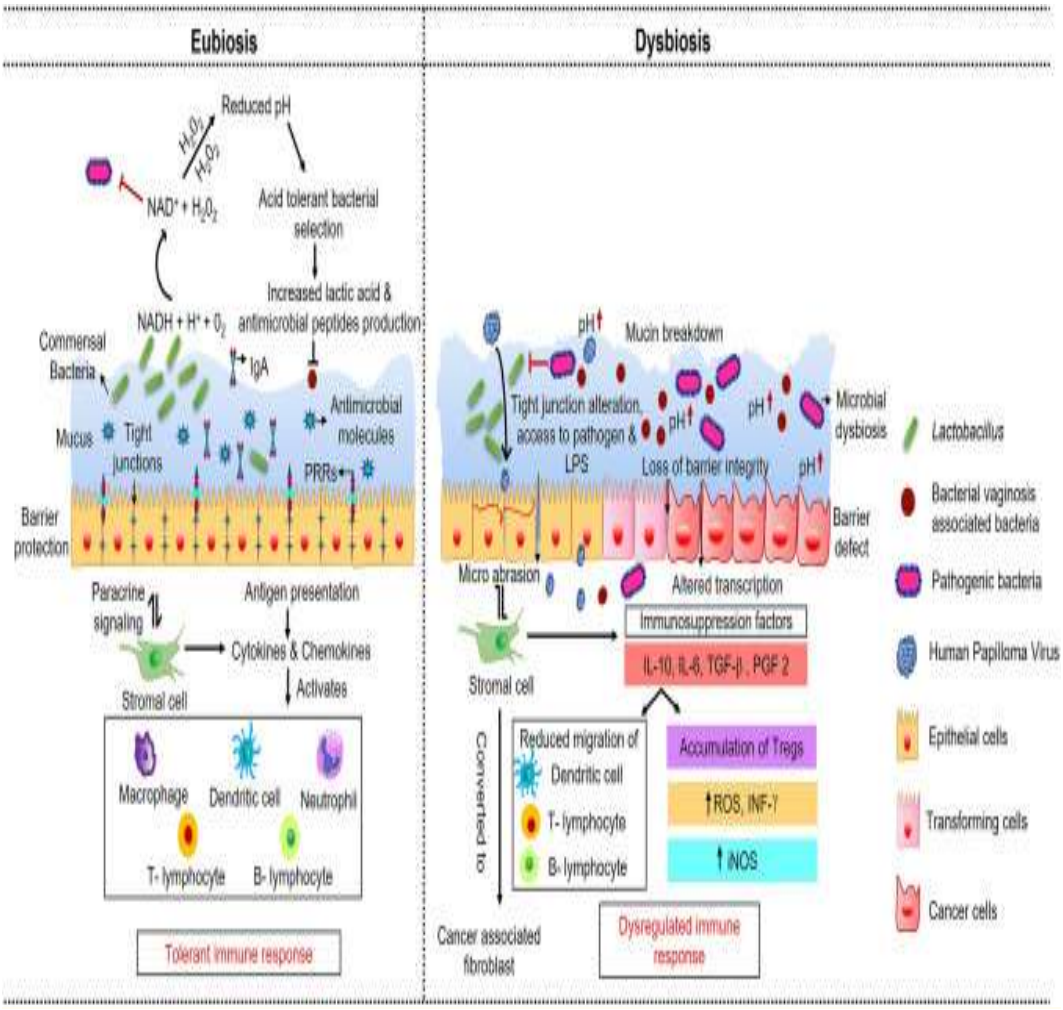
Figure 1: Shows the anatomical site of cervical cancer origin and the HPV-mediated evolution of the disease between aggressive squamous cell carcinoma and healthy cervix.
A) Diagrammatic representation of the female reproductive system
B) A diagram showing how HPV infection and the development of cervical cancer are related.

Adapted from https://images.app.goo.gl/wRQS22TJkRUnFAbDA

During SCC progression and HPV infection, Cervical intraepithelial neoplasia (CIN)is a dysplastic change in cervical epithelium's squamous cells **[8, 9]**. The majority of HPV infections resolve within a few years of exposure with only 10–20% of chronic infection potentially leading to cervical cancer **[10]**. Additionally, E5 contributes to the immunological neglect of infected host cells by reducing the expression of the surface receptors CD1d and major histocompatinility complex (MHC) classes I and II **[11-14]**. by blocking cellular checkpoints and interacting with host factors including tumor suppressors and promoters, E6 and E7 contribute to the development of cervical cancer **[15, 16]**. CIN1 is distinguished by mid dysplasia that includes koilocytes, binucleate cells, and dyskeratotic cells. Two thirds of the epithelium is affected by the many lesions that make up CIN2. More than two-thirds of the epithelium is affected by CIN3, a marker of severe dysplasia **[9]**. The most extensively used staging method for invasive cervical cancer is the International Federation of Gynaecology and Obstetrics (FIGO) recommendation, classified into stages I, II, III, and IV **(Table 1) [17]**. It is important to note that the transition from prenasive CIN to invasive cervical cancer might take 10-30 years.

ETHIOLOGY OF CERVICAL CANCER METASTASIS DYSREGULATION OF CERVICAL BIOME:

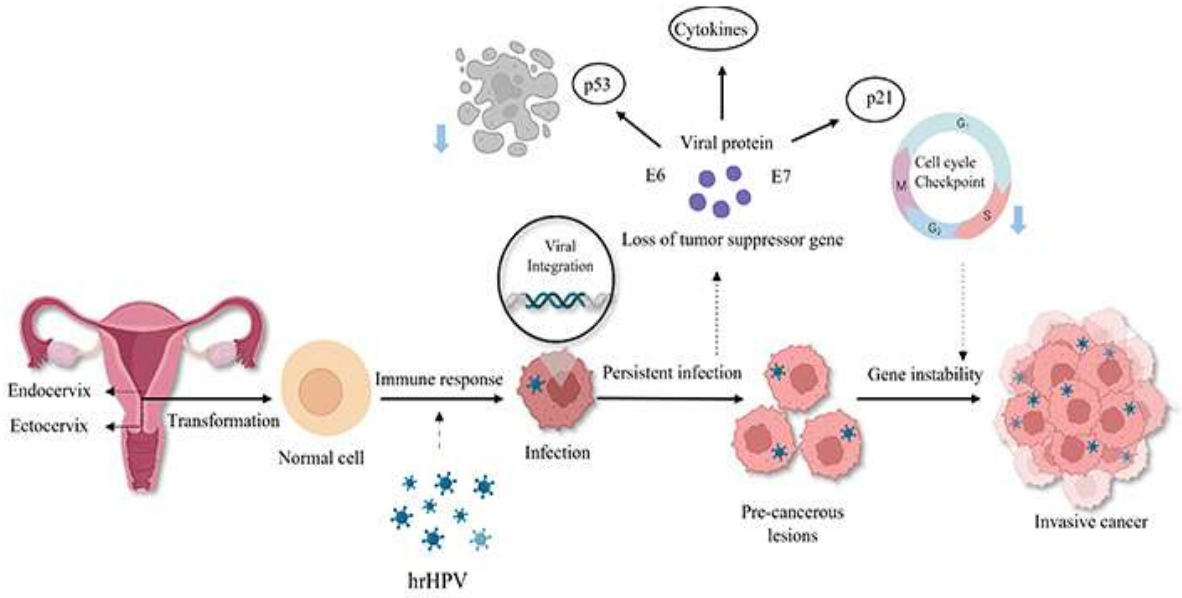
It has been shown that the dysbiosis of the cervicovaginal microbiome, when combined with HPV infection, is connected to the onset of CC **[18, 19]**. On the cervix's epithelial lining, immunocompetent cells control the immune system at the cervical area of the uterus **[20]**. In this area, innate and adaptive immunity are tightly regulated to maintain a balance between tolerance for commensal bacteria and the capacity to mount a quick defense against microbial invaders. Disruption of these coordinated cellular interactions during CC development results in a reduced immune response and low-grade chronic inflammation that is linked to an increased susceptibility to bacterial and viral infection at different stages of CIN. **Figure 1 [21]**.



Adapted from: https://images.app.goo.gl/c6fpTdjnVaeaksVm9

PATHOPYSIOLOGY OF CERVICAL CANCER:

Cervical cancer often develops only in cases of high-risk HPV infection. But HPV infection by itself cannot cause neoplasia to occur. Cervical intraepithelial neoplasia (CIN) is not a result of most high-risk HPV infections, which are usually transient. Cervical cancer occurs in a tiny proportion of women with high-risk HPV infections. A weakened immune system, HIV infection, and cigarette smoking are risk factors for HPV persistence **[22-25]**.



Adapted from: https://images.app.goo.gl/ALqy9fhvV9gj1Muy8

STRATEGIES USED TO PREVENT CERVICAL CANCER:

The Pap test and other HPV tests are considered secondary procedures, per guidelines from the World Health Organisation and other sources. A colposcopy and corresponding biopsy will be part of the next HPV DNA test procedure if the results are positive or abnormal **[26]**. A second HPV DNA test is recommended after a year, and thereafter testing every 12 to 24 months if the results of the cytological examination and the HPV test results do not agree.Patients who have a histological diagnosis of CIN2 should also receive surgical treatment along with focused continued surveillance **[27]**. Over the past fifty years, there has been a notable decrease in the incidence of cervical cancer in Europe, North America, Australia, and Japan thanks to the introduction of systematized cytology-based cervical screening programs in these regions **[28]**. Adopting and implementing the suggested plan is anticipated to reduce the median incidence rate by 42% by 2045 and 97% by 2120, according to the analytical model created by strategy developers **[29]**.

FIRST LINE DEFENSE:

Disseminating knowledge about safe sexual practices and advocating for HPV vaccination are examples of primary prevention **[30]**. According to available data, the two vaccination doses may be just as effective as three short courses in terms of effectiveness. This finding has significant ramifications for areas where cost barriers prevent people from getting vaccinated **[31]**. Beyond preventive vaccinations, therapeutic vaccines aim to eradicate HPV infections by

incorporating T-cell-mediated immunity against the virus's E6 and E7 antigens **[32]**.

SECONDARY DEFENSE:

By screening asymptomatic individuals or doing conclusive testing on symptomatic or screen-positive patients, secondary prevention aims to identify precancerous lesions before they progress to cancer. Cervical cancer screening comes with a lot of alternatives. Cervical cytology, which includes both liquid-based and conventional techniques, is one of the techniques used to screen for preinvasive illnesses. (2) visual inspection by direct observation; (3) Acetic acid visual inspection; (4) acetic acid visual inspection; (5) Lugol's iodine visual inspection; (6) HPV DNA testing; (7) speculoscopy; and (8) polar probes **[33]**. In particular project circumstances, other screening techniques are usually used.

TECHNOLOGY FOR PREVENTING CERVICAL CANCER:

HPV DNA analysis, thermal ablation for the treatment of precancerous lesions, and digital health initiatives are examples of novel cervical cancer preventative strategies. These advancements are intended to enhance the quality of care and treatment, as well as the precision, effectiveness, and economics of identifying women who are at risk of cervical cancer. For instance, the WHO-endorsed method of thermal ablation, which employs heat beams to destroy precancerous cervical lesions, holds great potential for preventing cervical cancer. Worldwide, these advancements in technology have led to the prevention and control of cervical cancer **[34]**.

TARGETED THERAPY IN CERVICAL CANCER:

Chemotherapy drugs cause crippling side effects like baldness and anemia by killing both cancer cells and healthy cells that divide quickly **[35]**. The purpose of targeted therapy is to prevent the growth, proliferation, and spread of cancer by blocking substances, usually proteins, that are expressed only by cancer cells. Since targeted therapies have a higher specificity for cancer cells than normal cells, it is expected that they will be more effective and have fewer side effects than current chemotherapies **[36]**. As a major obstacle in the present treatment paradigm, targeted therapy also seeks to address the mechanisms underlying tumor drug resistance **[35, 37, 39]**. The main oncogenic mechanisms that are most frequently targeted in cervical cancer treatment are covered in the sections that follow.

NEW STRATEGIES FOR CERVICAL CANCER PREVENTION WITH HPV VACCINES:

Cervical cancer incidence has been shown to be reduced by almost 90% by the human papillomavirus (HPV) vaccine; however,

only about 60% of adult women received the HPV vaccine. 2 NYU Langone researchers, including Catherine Herrman, MD, investigated whether immunising women of reproductive age against HPV could increase vaccination rates.

According to the study, offering HPV vaccinations in clinics that perform abortions is a sensible way to increase the number of patients who receive the vaccine and, when they become older, reduce their risk of developing cervical cancer.

CONCLUSION

The worldwide prevalence of cervical cancer is significant, and it continues to provide a substantial therapeutic challenge, particularly with poor and moderate incomes nations when assets grow scarce and available treatments are frequently expensive and out of reach. The World Health Assembly declared in 2020 that the following three goals must be met in order to "eliminate cervical cancer" by 2030: 90% of girls by the age of 15 are vaccinated against HPV, 70% of women are screened with high-performance tests at 35 and 45 years old, 90% of invasive cancer cases are managed, and 90% of precancerous lesions are treated **[38]**. Finding publicly accessible non-cancer medicines that concentrate on the ng elements is one tactic that could lead to the rapid and economical creation of new drugs.Finding more effective medications with noticeably fewer side effects should be the goal of a specialised approach involving drug repurposing. Furthermore, it is expected that these medications would swiftly advance to clinical trials due to their well-established safety profiles.

REFERENCES:

[1] Sekar PK, Thomas SM, Veerabathiran R: The future of cervical cancer prevention, advances in research and technology, Exploration of Medicine,5(3), 2024 ,384-400.

[2] Ganesan S, Subbiah VN, Michael JC: Associated factors with cervical pre-malignant lesions among the married fisher women community at Sadras, Tamil Nadu. Asia-Pacific journal of oncology nursing, 2(1), 2015 ,42-50.

[3] Bhatla N, Meena J, Kumari S, Banerjee D, Singh P, Natarajan J: Cervical cancer prevention efforts in India, Indian Journal of Gynecologic Oncology, 19(3), 2021,41.

[4] Wu J, Zhao Y, Li F, Qiao B. MiR-144-3p: a novel tumor suppressor targeting MAPK6 in cervical cancer, Journal of physiology and biochemistry,75(4) 2019, 143-52.

[5] Kombe Kombe AJ, Li B, Zahid A, Mengist HM, Bounda GA, Zhou Y, Jin T: Epidemiology and burden of

human papillomavirus and related diseases, molecular pathogenesis, and vaccine evaluation, Frontiers in public health,6(9), 2021, 552-28.

[6] Shin MB, Liu G, Mugo N, Garcia PJ, Rao DW, Bayer CJ, Eckert LO, Pinder LF, Wasserheit JN, Barnabas RV: A framework for cervical cancer elimination in low-and-middle-income countries, a scoping review and roadmap for interventions and research priorities, Frontiers in public health, 9(4), 2021, 670-732.

[7] Bermudez A, Bhatla N, Leung E: Cancer of the cervix uteri, International Journal of Gynecology & Obstetrics,13(7), 2015, 88-95.

[8] Small Jr W, Bacon MA, Bajaj A, Chuang LT, Fisher BJ, Harkenrider MM, Jhingran A, Kitchener HC, Mileshkin LR, Viswanathan AN, Gaffney DK. Cervical cancer: a global health crisis, Cancer,123(13), 2017, 2404-12.

[9] Balasubramaniam SD, Balakrishnan V, Oon CE, Kaur G: Key molecular events in cervical cancer development, Medicina, 55(7), 2019, 384.

[10] Shanmugasundaram S, You J: Targeting persistent human papillomavirus infection, Viruses, 9(8), 2017, 229.

[11] Miura S, Kawana K, Schust DJ, Fujii T, Yokoyama T, Iwasawa Y, Nagamatsu T, Adachi K, Tomio A, Tomio K, Kojima S:CD1d, a sentinel molecule bridging innate and adaptive immunity, is downregulated by the human papillomavirus (HPV) E5 protein, a possible mechanism for immune evasion by HPV, Journal of virology,84(22), 2010, 614-23.

[12] Zhang B, Li P, Wang E, Brahmi Z, Dunn KW, Blum JS, Roman A: The E5 protein of human papillomavirus type 16 perturbs MHC class II antigen maturation in human foreskin keratinocytes treated with interferon-γ, Virology,310(1), 2003, 100-108.

[13] Ashrafi GH, Haghshenas M, Marchetti B, Campo MS: E5 protein of human papillomavirus 16 downregulates HLA class I and interacts with the heavy chain via its first hydrophobic domain, International journal of cancer,119(9), 2006, 2105-12.

[14] Cortese MS, Ashrafi GH, Campo MS: All 4 di-leucine motifs in the first hydrophobic domain of the E5 oncoprotein of human papillomavirus type 16 are essential for surface MHC class I downregulation

activity and E5 endomembrane localization, International journal of cancer, 127(2), 2010, 1675-82.

[15] Balasubramaniam SD, Balakrishnan V, Oon CE, Kaur G: Key molecular events in cervical cancer development, Medicina, 55(7), 2019, 384.

[16] Pal A, Kundu R: Human papillomavirus E6 and E7, the cervical cancer hallmarks and targets for therapy, Frontiers in microbiology, 10(5), 2020, 3116.

[17] Pecorelli S: Corrigendum to "Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium" [International Journal of Gynecology and Obstetrics, International Journal of Gynecology and Obstetrics, 105(6), 2009,103-104.

[18] Castanheira CP, Sallas ML, Nunes RA, Lorenzi NP, Termini L: Microbiome and cervical cancer, Pathobiology,88(2), 2021,187-197.

[19] Klein C, Kahesa C, Mwaiselage J, West JT, Wood C, Angeletti PC: How the cervical microbiota contributes to cervical cancer risk in sub-Saharan Africa, Frontiers in Cellular and Infection Microbiology, 21(10), 2020, 23.

[20] Wira CR, Grant Tschudy KS, Crane Godreau MA: Epithelial cells in the female reproductive tract, a central role as sentinels of immune protection, American journal of reproductive immunology, 53(2), 2005, 65-76.

[21] Balasubramaniam SD, Balakrishnan V, Oon CE, Kaur G: Key molecular events in cervical cancer development, Medicina, 55(7), 2019,384.

[22] Stumbar SE, Stevens M, Feld Z: Cervical cancer and its precursors, a preventative approach to screening, diagnosis, and management, Primary Care, Clinics in office practice, 46(1), 2019, 117-34.

[23] Santamaría-Ulloa C, Valverde-Manzanares C: Inequality in the incidence of cervical cancer, Costa Rica 1980–2010, Frontiers in oncology,13(6), 2019, 664.

[24] Chrysostomou AC, Stylianou DC, Constantinidou A, Kostrikis LG: Cervical cancer screening programs in Europe, the transition towards HPV vaccination and population-based HPV testing, Viruses,10(12), 2018,729.

[25] Cheng L, Wang R, Yan J: A review of urinary HPV testing for cervical

cancer management and HPV vaccine surveillance: rationale, strategies, and limitations, European Journal of Clinical Microbiology & Infectious Diseases,5(8), 2024,1-2.

[26] Cascardi E, Cazzato G, Daniele A, Silvestris E, Cormio G, Di Vagno G, Malvasi A, Loizzi V, Scacco S, Pinto V, Cicinelli E: Association between cervical microbiota and HPV, could this be the key to complete cervical cancer eradication, Biology, 14(5), 2022, 1114.

[27] World Health Organization: WHO Guideline for Screening and Treatment of Cervical Pre-cancer Lesions for Cervical Cancer Prevention: web annex A, syntheses of evidence, In WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, web annex A: syntheses of evidence, 3(7), 2021,78-86.

[28] IARC Working Group on the Evaluation of Cancer-Preventive Strategies, International Agency for Research on Cancer, Cervix cancer screening, IARC, 76(7), 2005, 45-53.

[29] World Health Organization: Global strategy to accelerate the elimination of cervical cancer as a public health problem, World Health Organization,87(42),2020,786.

[30] Sekar PK, Thomas SM, Veerabathiran R: The future of cervical cancer prevention, advances in research and technology, Exploration of Medicine, 5(3)2024,384-400.

[31] Kitchener HC, Denton K, Soldan K, Crosbie EJ: Developing role of HPV in cervical cancer prevention, BMJ, 48(4), 2013,347.

[32] Solomon D, Castle P, Hildesheim A, Katki HA, Schiffman M, Wacholder S: HPV vaccination in women aged 24–45 years, The Lancet, 374(9697), 2009, 1239.

[33] Banerjee D, Mittal S, Mandal R, Basu P: Screening technologies for cervical cancer, Overview, Cytojournal,7(5),2022,19.

[34] Brown AJ, Trimble CL: New technologies for cervical cancer screening, Best practice & research Clinical obstetrics & gynaecology, 26(2), 2012, 233-42.

[35] Chabner BA, Roberts Jr TG; Chemotherapy and the war on

cancer: Nature Reviews Cancer,5(1), 2005,65-72.

[36] Tsuda N, Watari H, Ushijima K: Chemotherapy and molecular targeting therapy for recurrent cervical cancer, Chinese Journal of Cancer Research,28(2), 2016,241.

[37] Gottesman MM, Fojo T, Bates SE: Multidrug resistance in cancer, role of ATP–dependent transporters, Nature reviews cancer, 2(1),2002, 48-58.

[38] Canfell K: Towards the global elimination of cervical cancer, Papillomavirus research, 8(5), 2019, 1001-70.

[39] Vasantha G and Kiranmai S; Navigating the Complexities of Cancer Drugs: Understanding the Side Effects and Treatment Strategies, 15 (85), 2024, 78833-78846.