IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

# A Review On: Comprehensive Insights Into HPV And Cervical Cancer Prevention.

[1]Devika Yashwant Karale, [2]Nupur Shashipal Hiwale,

Shani Soham Apartment, B- wing 502, Morvali Pada, Ambernath East, India, 421501.

***Abstract:*** Cervical cancer is a significant global health burden, predominantly caused by persistent infection with high-risk types of human papillomavirus (HPV). Cervical cancer remains a significant global health challenge, particularly in low and middle-income countries where access to preventive measures and healthcare resources are limited. This article provides a concise overview of the epidemiology, pathogenesis, and prevention strategies related to cervical cancer and HPV. A holistic approach encompassing prevention, early detection, utilization of diverse screening techniques, and treatment measures can effectively prevent and treat cervical cancer.

***Keywords:*** Cervical cancer, Human papillomavirus (HPV), HPV negative cervical cancer, vaccine

## I. INTRODUCTION

Cervical cancer is the second most common cancer among women in the reproductive age group according to World Health Organization. Human papillomavirus (HPV) causes Cervical cancer. In India, cervical cancer poses a significant public health concern, underscoring the importance of raising awareness among women about risk factors and preventive measures. The purpose of the review is to comprehensively analyze the current body of research surrounding human papillomavirus strains known to cause cancer, with a focus on diagnostic methods, treatment modalities, and prevention strategies associated with HPV-induced cancers. By synthesizing and critically evaluating existing literature, this review aims to provide a comprehensive understanding of the multifaceted aspects of HPV- induced cancers, this review will contribute to the advancement of strategies for the prevention, early detection, and management of HPV-associated cancers, thereby facilitating improved clinical outcomes and public health interventions. India has a population of 466.76 million women, aged 15 years and older, who are at risk of developing cervical cancer of which annually 1,22,844 women are diagnosed with cervical cancer and 67,477 die.

***Human papillomavirus*:** HPV is a double-stranded circular DNA virus which consists of approximately 8000 base pairs there are more than 100 types of HPV out of which 15 are high-risk HPV types that cause cancer. HPV has a simple structure and is only built with a few genes i.e. six early and two late genes. The late genes L1 and L2 encode major capsid proteins and the early genes (E6, E5, E7, E1, E2, E4) control replication. Two of the early genes (E6 and E7) transformed squamous epithelium into cancer they have the ability to immortalize cells.

HPV belongs to the papillomaviridae family it is a small, non-enveloped, double-stranded DNA viruses. HPV target epithelial cells of oral, skin, and anogenital mucosa. There are around 53 genera in the family papillomaviridae from which 5 genera (alphapapillomaviruses, betapapillomaviruses, gammapapillomaviruses, mupapillomaviruses and nupapillomaviruses) are associated with HPVs. More than 200 types of HPV have been identified by the International HPV Reference Center. HPV types are classified into two categories low risk and high risk. A group of 15 high-risk HPV types is responsible for causing cervical cancer, as well as vulvar, vaginal, penile, and oropharyngeal cancers. HPV types 6 and 11 are responsible for genital warts. There are additional types of HPV that can lead to cancer, but these are less prevalent. HPV-16 AND HPV-18 are responsible for causing 70% -80% of the total cases of cervical cancer. Based on Indian studies, about 82.7% of invasive cervical cancers have shown the presence of HPVs 16 or 18. HPV infection is limited to the basal cells of the epithelium. Uncontrolled cell proliferation and mutation give rise to HPV lesion, which can ultimately lead to cancer. Most Of the HPV infection do not cause symptoms and resolve spontaneously within 1 or 2 years; while those women who develop cervical cancer can test positive prior to cancer.

***Classification of HPV types by IARC***

| **Classification** | **HPV types** |
|---|---|
| Group 1 carcinogenic (high-risk) | 16,18,31,33,35,39,45,51,52,56,58,59 |
| Group 2A is probably carcinogenic (high-risk) | 68 |
| Group 2B is possibly carcinogenic (intermediate risk) | 25,53,67,70,73,82 |
| Group3 (low risk) | 6,11,40,42,43,54,61,81,89,90 |

***Cervical cancer:*** Cervical cancer is one of the most common causes of cancer deaths in women globally. The cervix is located between the vagina and uterus, characterized by the simple columnar secretory epithelium. The area in which over 90% of lower genital tract malignancies initiate is the squamocolumnar junction is vulnerable to transformation by high-risk HPV. Cervical cancer can occur in two different forms as there are two types of epithelial cells found in the transition zone (squamous and glandular cells). HPV infects basal epithelial cells through the epithelial abrasion and induces cervical dysplasia and CIN (cervical intraepithelial neoplasia) which later develop into cancer due to persistent infection of high-risk HPV A significant 96% of cervical cancers are linked to the 13 HPV types classified in groups 1 and 2A.

Persistent HPV infection is a critical factor in the progression of cervical cancer. The competition between persistence and clearance is central to HPV carcinogenesis. As precancerous lesions advance, the immune system responds by recruiting CD4+, CD8+, lymphocytes as well as macrophages, increasing levels of proinflammatory cytokines, and stimulating the production of neutralizing antibodies. The immune response to the infection is gradual and results in low antibody levels. The neutralizing antibodies are triggered after

viral infection and target viral particles instead of virus-infected cells, which does not cure infection. The effector T cells target early viral proteins eliminating virus-infected cells.

***HPV-negative cervical cancer:*** Invasive cervical cancer (ICC) (cancer that has spread beyond the surface layer of the cervix and into the deeper tissues) can be divided into three groups: squamous cervical cancer (SCC) which accounts for 75-90% of ICCs, adenocarcinomas (ADC) and adenosquamous cell carcinomas (ASC). Research indicates that nearly all cases of squamous cell carcinoma and a significant portion of adenocarcinoma (ADC) are positive for HPV infection, with SCC approaching 100% positive and ADC around 86%. Instances of HPV-negative cervical cancer are exceptionally rare. Various factors contribute to HPV negativity, including limitations in HPV detection methods, instances of cervical cancers not driven by high-risk HPV, tumors losing HPV expression over time, association with non-high-risk HPV types, and misclassification of cancers, such as mistaking uterine endometrioid adenocarcinoma or metastases from other primary tumors for cervical cancer. Common reasons for false-negative HPV results include issues with HPV tasting methods and misclassification of tumor types.

***HPV vaccine against cervical cancer:*** To thwart HPV infections that can lead to cancer, licensed bivalent, quadrivalent, and non-valent HPV vaccines have been rolled out in 125 countries. The primary focus for HPV vaccination in most of these nations is on adolescent girls, particularly those aged 9-14 years, before their sexual debut. To eliminate cervical cancer World Health Organization (WHO) has started all adolescent girls who are age 15 and should have received HPV vaccination by 2030.HPV vaccine works via binding to the virus which prevents infecting the epithelial tissues. Yet, the antibodies generated from natural infections typically fail to provide adequate protection against subsequent reinfection. This is because the cervical site, where infection occurs, lacks secondary lymphoid tissue housing numerous memory B cells, which are crucial for producing antibodies and neutralizing the virus before it can take hold. Moreover, to maintain a protective immune response throughout one's sexually active life, vaccination must elicit high and sustained levels of neutralizing antibodies. Thus, an optimal HPV vaccine should elicit an enhanced protective immune reaction, offering defense against all high-risk HPV strains as well as other potentially carcinogenic types. At present, the HPV vaccine relies on virus-like particles (VLPs), constructed from recombinant HPV capsid proteins, ensuring they are non-infectious as they lack viral DNA. As of now, there are three approved prophylactic HPV vaccines available

| Vaccine name | Type | Target |
|---|---|---|
| Gardasil | Quadrivalent (4vHPV) | HPV6, HPV11, HPV16, HPV18 |
| Cervarix | Bivalent (2vHPV) | HPV16 and HPV18 |
| Gardasil 9 | Non-valent (9vHPV) | HPV5, HPV11, HPV16, HPV16, HPV18, HPV31, HPV33, HPV45, HPV52, HPV58 |

The quadrivalent HPV vaccine (4vHPV) is recommended for females and males aged 9-26 years to prevent genital warts, precancerous or dysplastic lesions, and cervical cancer. Meanwhile, the non-valent (9vHPV) vaccine, which includes coverage for five additional types of HPV types, is authorized for females and males

aged 9-45 years to prevent genital warts, precancerous or dysplastic lesions, and cervical, vulvar, vaginal, and anal cancer. HPV vaccination offers significant potential in preventing cervical cancer, cervical intraepithelial neoplasia (CIN), and adenocarcinoma in situ. The natural immune response to HPV infection is not as strong compared to HPV vaccination, however, it is found that these vaccines provide limited benefits to eliminate pre-existing infection and elicit type-restricted protection. HPV vaccines need to contain a wide range of VLP types for broad protection.

Over 200 million doses of preventive vaccines have been given globally. As vaccination rates have increased safety concerns have arisen, including common side effects like arm pain, redness, swelling, fever, headache, fatigue, nausea, and muscle or joint pain. Before FDA approval in 2014, seven studies assessed the safety of the 9vHPV vaccine, finding it comparable to the 4vHPV vaccine in terms of safety profile. Administering the HPV vaccination before, during, or shortly after pregnancy does not appear to increase the risk of adverse pregnancy outcomes, according to studies. While it is not advised for pregnant women, those who are breastfeeding can safely receive the vaccine. It's important not to panic if a woman inadvertently receives the HPV vaccine during pregnancy. Prophylactic HPV vaccines work by stimulating the immune system to produce antibodies against specific late proteins, L1 OR L2 which ultimately neutralizes the antigens. Therapeutic vaccines primarily target the elimination of precancerous lesions and persistent HPV infections. These vaccines focus on antigens like the early proteins E6 and E7, which are consistently expressed in HPV-related infections and most cervical cancer cases while being absent in normal tissues. Over the last twenty years, a diverse range of therapeutic HPV vaccines has been extensively researched. These include vaccines utilizing live vectors, nucleic acid/protein/peptide-based formulations, as well as cell-based approaches.

***Barriers to HPV vaccine uptake among adolescent girls***

1. Perceived a low risk: parents perceived their daughters to have a low risk of acquiring HPV infection or developing cervical cancer, leading them to view the vaccine as unnecessary. Various factors contributed to the perception, such as the perceived low prevalence of HPV, absence of a family history of cervical cancer, considering the vaccination age as too early, or believing their daughters were not engaging in high risk sexual behavior.

2. Negative consequences: parents express concerns regarding potential side effects of the HPV vaccine, such as pain, allergic reactions, and other adverse effects, particularly if their daughter has compromised immune system. Additionally, they fear negative experiences associated with HPV vaccination, often influenced by others accounts. Another worry is that the vaccine might encourage risky sexual behavior in their daughters.

3. Inadequate effectiveness: parents held the belied that the HPV vaccine did not provide comprehensive and lasting protection against all strains of HPV.

4. Lack of trust: certain parents also felt that the vaccine was primarily introduced for financial gain. They harbored suspicions towards the government, medical establishment, and pharmaceutical companies.

5. Misinformation and lack of information: a Somali mother received misinformation from a healthcare provider who incorrectly advised her that HPV vaccination should be administered when her daughter reached reproductive age. Insufficient information about the vaccine, its dosing regimen, effectiveness backed by

statics, and the appropriate age for vaccination failed to convince parents to make informed decisions regarding vaccinating their daughters.

6. Medical practice models and idiosyncratic beliefs: some ethnic minority parents opted not to vaccinate their daughters due to their preference for natural immunity-building methods and idiosyncratic beliefs, such as preventing cervical cancer through healthy lifestyles and the belief that cervical cancer development is controlled by a higher power.

***Prevention***

1. Vaccination against HPV is highly effective in preventing cervical cancer.
2. Pap test is screening tests that can detect abnormal cells on the cervix before they developed into cancer. Regular screening can help detect cervical cancer early when it is most treatable
3. Practicing safe sex, such as using condoms and limiting sexual partners, can reduce the risk of HPV infection and other sexually transmitted infections that can contribute to cervical cancer.
4. Eating a healthy diet rich in fruits and vegetables, maintaining a healthy weight, and getting regular exercise may help reduced the risk of cervical cancer
5. Excessive alcohol consumption has been linked to an increased risk of cervical cancer, so limiting alcohol intake is advisable.
6. In addition to Pap tests, HPV testing can also help detect high-risk HPV strains that are associated with cervical cancer. HPV testing is often done in conjunction with Pap testing for women over 30.

***Result*:**

This review highlights the profound impact of human papillomavirus (HPV)

On cervical cancer, especially in countries like India, where healthcare resources are often limited. Persistent infection with high-risk HPV types, particularly HPV-16 and HPV-18, is the primary cause of most cervical cancer cases, with these strains being linked to more than 96% of cases. This review emphasizes the crucial role of HPV vaccines, in preventing these high-risk infections. The immune system's limited natural response to HPV infections highlights the greater reliability of vaccines in offering long-term protection. A concerned effort to integrate vaccination, routine screening, and awareness campaigns is essential to significantly reduce the burden of cervical cancer.

***Conclusion*:** Cervical cancer is one of the most preventable yet persistent health challenges worldwide, largely due to infections caused by high-risk HPV strains. Effective tools like vaccines and screening programs have already shown great promise in reducing the disease's impact, but their success is limited by barriers such as misinformation, access gaps, and social mistrust. To overcome these challenges, a united approach is needed that combines widespread vaccination, regular and accessible screening, and public health education to empower individuals and communities. By addressing barriers and ensuring equitable access to healthcare.

***Reference:***


1. Olaf Reich, Sigrid Regauer (2023). Elimination of reserve cells for prevention of HPV-associated cervical cancer. Virus Research, 10.1016/j.virusres.2023.199068
2. Jyoti Singh, Sulakshana S. Baliga (2021). Knowledge Regarding Cervical Cancer and HPV Vaccine among Medical Students: A Cross-Sectional Study. Clinical Epidemiology and Global Health (Volume 9). https://doi.org/10.1016/j.cegh.2020.09.012
3. Renjie Wang, Wei Pan, Lei Jin, et.al. (2020). Human papillomavirus vaccine against cervical cancer: Opportunity and challenge. Cancer Letters. https://doi.org/10.1016/j.canlet.2019.11.039
4. Finja Seifert, Rieke Eisenblätter, et.al. (2023). Association of two genomic variants with HPV type-specific risk of cervical cancer. Tumour Virus Research. https://doi.org/10.1016/j.tvr.2023.200269
5. Rebekah Pratt , Christina Bliss Barsness , John Lin, et.al. (2024). Integrating HPV self-collect into primary care to address cervical cancer screening disparities. Preventative Medicine Reports (Volume 38). https://doi.org/10.1016/j.pmedr.2024.102599