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Research Article

The Role of HPV Vaccine in Preventing Cervical Cancer

Baneen M. Obaid[1*], Saja H. Hashim[2], Tabark E. Jassim[3], Hind Z. Turki[4], Hajar J. Khazaal[5]

[1,2]Deparment of Pharmaceutical Chemistry, College of Pharmacy, University of Babylon, Babylon, Iraq

[3]Department of Pharmaceutics, College of Pharmacy, University of Babylon, Babylon, Iraq

[4]Department of Pharmacology and Toxicology, College of Pharmacy, University of Babylon, Babylon, Iraq

[5]Department of Pharmacognosy and Medicinal Plants, College of Pharmacy, University of Babylon, Babylon, Iraq.

Abstract:

Cervical cancer continues to be a significant health challenge worldwide, especially in resource-poor settings which account for over 90% of the deaths. Persistent infection with high-risk human papilloma virus (HPV) types, particularly HPV-16 and HPV-18, is the leading cause of cervical cancer. This review focuses on the HPV vaccines and their remarkable success in preventing cervical cancer since 2006. Prophylactic vaccines against HPV-16 and -18, as well as bivalent and quadrivalent vaccines, use virus-like particles (VLPs) to stimulate immune responses and have been shown to significantly reduce HPV infections, as well as cervical intraepithelial neoplasia and invasive cervical cancer. The review discusses vaccine functions and effectiveness, including their immunogenicity and ideal dosing intervals, as well as the advantages gained from early vaccination. These strides in vaccination are unfortunately not mirrored in other countries such as Iraq due to a lack of surveillance data, cultural concerns, and the absence of a national vaccination program. There remains a greater need for education, policy change, and infrastructure to support the roll-out of HPV vaccination programs. Further development into therapeutic HPV vaccines targeting the E6 and E7 oncoproteins may aid in future treatments for cancer. This review highlights the importance of comprehensive HPV vaccination in achieving these goals.

Keywords: HPV, cervical cancer, HPV vaccine, prevention, immunization, public health, virology, neoplasia

Introduction

Cervical cancer is considered as the fourth most prevalent cancer in women worldwide, continues to pose a serious challenge to global population health [1]. In 2022 specifically, It is attributed for over 350,000 fatalities, and more than 90% of cases reported in countries with limited economic resources where access to screening and immunization is restricted [2]. The impact of this disease is significantly associated with long-standing infection by potentially carcinogenic types of human papilloma-virus (HPV), which are responsible for approximately 70% of all cervical cancer cases especially types 16 and 18 [3].

As the causal link between HPV and cervical cancer has been widely recognized through decades of epidemiological and molecular research, that made the cervical cancer one of the few cancers that is effectively preventable in the future through vaccination campaigns [4]. When the prophylactic HPV vaccine was initially introduced in 2006, the national vaccination campaigns have been implemented in numerous countries with notable outcomes. HPV vaccination decreased HPV 16 and 18 infections in girls aged 13 to 19 by 83% and by 66% in women aged 20 to 24, according to a systematic review and meta-analysis with more than 60 million people [5].

The effectiveness of vaccine surpasses infection prevention which is supported by Real-world data. A Swedish cohort study showed that girls who received the quadrivalent HPV vaccine before age 17 had an 88% reduced risk of having invasive cervical cancer in comparing to unvaccinated individuals [6]. Cervical cancer incidence and cervical intraepithelial neoplasia (CIN3) have also significantly decreased in vaccinated populations, according to Danish registry data [7].

World Health Organization (WHO) is considering HPV vaccination as a foundation to eradicate cervical cancer now, in addition to screening and early intervention[8]. Promisingly, emerging evidence suggests that a single-dose HPV vaccine may provide long-lasting protection, potentially enhancing accessibility in low-resource settings [9]. This review explores the immunological principles of HPV vaccination, the effectiveness of different vaccine formulations and regimens, its impact on population-level cervical cancer trends, and ongoing challenges to global implementation.

HPV And Cerivical Cancer

Human papilloma virus (HPV), especially high-risk types such as HPV-16 and HPV-18, is the leading cause in the development of cervical cancer. The viral oncoproteins E6 and E7 interfere with fundamental tumor suppressor genes. As the oncoprotein E6 encourage the breakdown of p53 through its interaction with the ubiquitin ligase E6AP, disturbing apoptosis and DNA repair [10]. Simultaneously, E7 attaches to the retinoblastoma protein (pRb), releasing E2F transcription factors and inducing unregulated

progression of cell cycle division. [11]. These molecular actions lead to genetic alterations and cellular transformation. Additionally, HPV modulates host gene expression by altering miRNAs and lncRNAs [12], and the viral oncoprotein E5 promotes growth signals via EGFR pathways [13]. These molecular alterations demonstrates the foundation for neoplastic progression and emphasizes the value of prophylactic vaccination and regular screening.

Types of HPV Vaccines

By the year 2023, six different HPV vaccines are available worldwide, all of them offer protection against the high risk HPV types 16 and 18-responsible for nearly 70% of cervical cancer. These include three bivalent vaccines, two quadrivalent vaccines and one nonavalent vaccines [14].

Two HPV vaccines have been officially licensed in the USA . The first one, the bivalent vaccine (HPV2), known as *Cervarix* (GalaxoSmithkline) , is indicated for females aged 9 to 25 years old and targets HPV types 16 and 18 . The second one , which is the quadrivalent vaccine (HPV4), known as *Gardasil* (Merck) , is approved for both females and males between the age of 9 and 26 years. Its provide protection against HPV types 6, 11, and 18, including both high risk and low risk types associated with cervical cancer and genital warts[15].

The third type of vaccine , is the nonavalent HPV vaccine, which is known as *Gardasil 9* (9vHPV). This vaccine , developed by merck, offer protection against nearly nine HPV types; 6, 11, 16, 18, 31, 33, 45, 52, and 58. [16].

Based on structure, these vaccines contain virus-like particles (VLPs) know as the L1 protein, which is considered noninfectious. In the quadrivalent vaccine, the L1 protein is synthesized in Saccharomyces cerevisiae (baker's yeast), each 0.5 ml dose contains various amounts of L1 proteins for HPV types 6, 11, 16, and 18, instilled in an aluminum-based adjuvant (AAHS) to improve the immune response. As opposed to , the bivalent vaccine contain L1 proteins which are produced in insect cells (Trichoplusia ni Hi-5),for each dose including 20 µg of L1 protein for HPV-16 and HPV-18. The aiding formulation in this vaccine composed of aluminum hydroxide and monophosphoryl lipid A (MPL), which helped increase duration and strength of immune protection. [15].

Compared to the original Gardasil vaccine, Gardasil 9 contains extreme quality of both antigen and aluminum adjuvant . Particularly, it contains large amount of L1 virus-like particles (VLPs) for HPV types 16 and 18 to confirm that the immune system response is not less than that produced by Gardasil [17].

Mechanism of Action of the HPV Vaccines

1. The HPV vaccine is produced by using virus-like particles (VLPs) derived from the L1 major capsid protein of the human papilloma virus. These particles resemble the structure of the natural virus but include no genetic material, making them non-infectious. This structural mimicry permits the immune system to recognize the VLPs as foreign, triggering a strong immune response [18].
2. Upon administration, the VLPs are taken up by antigen-presenting cells (APCs), such as dendritic cells, at the injection site. These APCs process the L1 protein and present it to helper T cells ($CD4^+$), which then stimulate B cells to produce high-affinity neutralizing antibodies specific to the HPV types in the vaccine [19].
3. The neutralizing antibodies generated target conformational epitopes on the surface of HPV, particularly those found on the L1 protein. These antibodies bind to incoming HPV virions and prevent their attachment to the basal epithelial cells of the cervix, thereby blocking initial infection [20].
4. Long-term follow-up studies have demonstrated that these antibody responses remain elevated for years post-vaccination, with immunity persisting for more than ten years in many cases. Memory B cells maintain immune readiness, enabling a rapid response upon re-exposure to the virus [21].
5. Although the vaccine primarily induces a humoral response, limited activation of T cells, especially $CD4^+$ T cell–driven cytokine secretion (e.g., IFN-γ, IL-2), has also been observed and may play a supportive role in the antibody response. However, cytotoxic $CD8^+$ responses are minimal in prophylactic vaccines [22].
6. One notable benefit of the HPV vaccine is cross-protection, offering immunity beyond the targeted HPV strains. Antibodies produced against vaccine-included types (e.g., HPV-16 and 18) may also neutralize phylogenetically related types like HPV-31 and 45 due to structural similarities in the L1 protein [23].
7. These antibodies are also found in cervical mucus, where they help strengthen the mucosal immune response at the site of viral entry. Transudation of IgG antibodies across mucosal surfaces contributes to preventing infection at the point of entry [24].
8. Additionally, recent findings suggest that the Fc region of these antibodies can mediate immune effector functions such as antibody-dependent phagocytosis and complement activation, further enhancing vaccine efficacy [25].

Recommended Dose

Children at ages of 11 and 12 should obtain two HPV vaccination doses seperated by six to twelve months. at age 9, HPV vaccinations can be administered also. If the first dose was received before to the 15th birthday, then only two doses are required. A third dose of the HPV vaccine is required for children aged 9 to 14 who have received two doses within five months of one another. Three doses of the HPV vaccine are required for those aged 15 to 26 who begin the series later. Individuals at ages of 9 to 26 who have compromised immune systems should receive three doses [26].

Effectiveness in Cervical Cancer Prevention

The impact of achieving high vaccination coverage among preadolescent girls on cervical outcomes was the primary focus of early cost-effectiveness studies . However, it has since been suggested that vaccination should be extended to women up to the age of 30 or even 45–50. Further modeling has indicated that, if uptake is high in both sexes, vaccination of older women and boys may yield benefits that are comparable to or even greater than those obtained by vaccination of preadolescent girls [27]. Numerous investigations have demonstrated a correlation between the quantity of vaccine doses and their efficacy and immunogenicity, and the results of a single HPV vaccination dose lead to decreased serum antibody titers. In order to prevent oral HPV infection, a single dose of the vaccine may not be as effective as two or three doses; receiving three doses maximizes the vaccine's effectiveness [28].

According to other research, in a high coverage setting, one dose was just as effective at preventing high-grade disease as two or three doses. These results lend credence to the idea that a one-dose vaccination might be a practical approach to the worldwide eradication of cervical cancer [29].

Gardasil 9 (9-valent) single-dose vaccinations simplify vaccine delivery, lower costs, and ease vaccine supply constraints while offering comparable health benefits to two-dose vaccinations. If there is a high incidence of cervical cancer, a shorter duration of protection from a single dose, a less expensive vaccine, and vaccination delivery methods, the second dose might be more economical [28].

Studies show that vaccines are more effective when they're given at younger ages, and the effectiveness might be diminished when administered at older ages [30].

Health care promotion most be focus on adherence to recommend schedules and timely vaccinations . Appropriate doses of vaccine against this virus can be inexpensively administered even in developing or underdeveloped countries. However, the successful and timely (appropriate age) administration of vaccinations will be significantly helped by educating and increasing awareness among people. Healthcare providers can enhance the vaccine's ability to offer long-term protection against HPV-related health risks by starting vaccination at younger ages and following the recommended number of doses based on age groups [28].

Challenges and Limitations

In this review, a thoughtful and thorough approach was used to explore the role of the human papilloma virus (HPV) vaccine in preventing cervical cancer, with a particular focus on the situation in Iraq. The research involved analyzing literature published between 2006 and 2025, sourced from respected international databases such as Pub-med, Scopus, and Google Scholar. Where available, regional journals and reports from Iraq's Ministry of Health were also included to capture local context [31]. The studies chosen covered a wide range of topics including HPV infection rates, vaccine safety and effectiveness, strategies for implementation, public acceptance, and the potential influence of vaccination programs on reducing cervical cancer cases and deaths. Given the lack of extensive research specific to Iraq, information from other countries in the Middle East and North Africa (MENA) region with similar socioeconomic conditions was also considered to help fill in the gaps. Both quantitative data and qualitative insights were brought together to better understand the current landscape and to shape recommendations that could support public health efforts in Iraq moving forward [32].

Methodology

While the methodology provided a solid foundation for this review, several limitations were identified along the way. One of the most significant issues is the limited availability of reliable national data on HPV infection rates, types of the virus found in Iraq, and how common cervical cancer actually is. Most of the existing research is based on hospital-level data, which often reflects only a narrow segment of the population and may not represent national trends. Another major gap is the absence of a national cancer registry in Iraq, which makes it even more difficult to track the disease or measure the long-term impact of any vaccination efforts. Beyond data challenges, there are also deep-rooted cultural and societal barriers that make discussing sexually transmitted infections like HPV a sensitive topic. This often leads to low levels of awareness, not only among the general public but also within the healthcare community. Additionally, Iraq does not yet have a nationwide HPV vaccination program [33]. Limited access to the vaccine, logistical difficulties in distribution, lack of funding, and weak infrastructure all contribute to making the implementation of such programs particularly difficult. Unless these issues are addressed through targeted awareness campaigns, stronger policies, and cross-sector collaboration, progress in preventing cervical cancer through HPV vaccination will remain slow. It's crucial for health officials, medical professionals, and community leaders to work together to create solutions that are both effective and culturally appropriate for the Iraqi population [34].

Conclusion

It is justified to develop therapeutic HPV vaccines since high-risk HPV has been identified as the causative agent of numerous diseases. Recent advancements in the field, including those covered in this review, have contributed to the foundational effort to eradicate HPV and diseases and cancers linked to HPV. We covered the different approaches to targeting HPV oncoproteins E6 and E7 in this review. These proteins are tumor-specific antigens and make good targets for therapeutic HPV vaccines. The present

therapeutic HPV vaccines listed in this review, in our opinion, each have benefits and drawbacks. The anti-tumor efficacy of therapeutic HPV vaccines still needs to be confirmed by more clinical research.

Over the coming years and beyond, we expect therapeutic HPV vaccines to remain effective due to continuous efforts to enhance and create therapeutic treatment approaches. In addition to other treatments currently available for the management of HPV-associated diseases, we anticipate that therapeutic HPV vaccines will soon be made clinically available.

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