Effectiveness of HPV Vaccine in Cervical Cancer Prevention: A Literature Review

Rahma Khaerussifa[1], Agustina Tri Pujiastuti[1]

[1]Faculty of Medicine, Universitas Pembangunan Nasional Veteran Jawa Timur

Corresponding author:
Rahma Khaerussifa
Faculty of Medicine, Universitas Pembangunan Nasional Veteran Jawa Timur
Rungkut Madya Number 191, Rungkut Kidul, Rungkut, Surabaya, East Java 60293
Tel/Fax: +6282260834119
E-mail: 23091010034@student.upnjatim.ac.id

Abstract

Cervical cancer is one of the leading causes of death in women worldwide, with more than 600,000 cases and 342,000 deaths occurring in 2020. The World Health Organization (WHO) has set a global strategy to eliminate cervical cancer by 2030, where Human Papillomavirus (HPV) vaccination is one of its main pillars. In Indonesia, the HPV vaccination program has been implemented as a preventive measure in preventing cervical cancer, with the main target being girls aged 9 to 14 years. HPV vaccines, especially types 16 and 18, have been shown to be effective in preventing more than 70% of cervical cancer cases. This literature review evaluates the effectiveness of the HPV vaccine for girls in Indonesia and the challenges in its implementation. Although the national vaccination program has been successfully implemented in various regions, challenges such as socio-economic, myths about vaccines, and rejection from parents are still obstacles in achieving optimal vaccination coverage. Continuous education to the public is essential to build a better understanding of the benefits of HPV vaccination in preventing cervical cancer. With higher vaccination coverage, it is hoped that the incidence rate of cervical cancer can be significantly reduced in the future.

Keywords: HPV Vaccine, Effectiveness, and Cervical Cancer

Introduction

Cancer is a non-communicable disease, but globally it has infected more than 19.3 million people and caused about 10 million deaths. According to a WHO report, cervical cancer is one of the most feared types of cancer for women, besides breast cancer. In Indonesia, around 9.3% of all cancer cases are cervical cancer. In Riau Province, cervical cancer ranks third after breast and ovarian cancer in 2019. Based on a report by the Riau Province Arifin Achmad Hospital in 2020, the number of new cases and deaths due to cervical cancer at the hospital has increased every year from 2016 to 2019. The Case Fatality Rate (CFR) of cervical cancer in 2016 was recorded at 5.88%, increasing to 10.36% in 2017, 17.30% in 2018, and 17.37% in 2019. [1]

WHO also noted that HPV (human papilloma virus) infection is a major risk factor for cervical cancer. Currently, more than 200 types of HPV have been identified, with 30 to 40 types capable of infecting the epithelial lining of the cervix of the HPV divided into three groups, namely low-risk HPV (HPV), potential high-risk HPV (HPV), and high-risk HPV (HPV). High-risk HPV types are the leading cause of pre-cancerous infections and invasive cervical cancers (Nita and Novi Indrayani, 2020). [1]

WHO Director-General, Dr. Tedros Adhanom Ghebreyesus, called for concrete actions to eliminate cervical cancer. Support for the WHO's global strategy to achieve formal elimination was announced on 17 November 2020, with a target of vaccinating 90% of girls with the HPV vaccine by the age of 15, and 70% of women undergoing cervical cancer screening by the ages of 35 and 45 by 2030.

In 2020, more than half of WHO member countries have launched HPV vaccination programs as a step towards achieving the target of cervical cancer elimination in the Sustainable Development Goals by 2030, which includes 90% elimination. Universal access to HPV vaccination will be a key factor in lowering the burden of cervical cancer worldwide. [3]

Method

This research method uses a literature review approach, which aims to collect and synthesize research results related to the effectiveness of HPV vaccine in the prevention of cervical cancer. Inclusion criteria include studies published in the last 5 years, while review articles and irrelevant ones are excluded.

Discussion

Human papillomavirus (HPV) is a small DNA virus belonging to the genus Papillomavirus of the family Papovaviridae. This virus has a circular DNA closed with two strands (double-stranded), does not have a sheath, and is equipped with an isohedral capsid consisting of 72 capsomers. The diameter of this virus is about 55 micrometers with a molecular weight of about 5 x 10^6 Daltons. The HPV genome is relatively small, with a size of about 8 kb, and encodes 8 genes. These genes are made up of 6 early-expressed non-structural proteins, known as early genes, namely E1, E2, E4, E5, E6, and E7, which are related to the regulation of DNA replication and cell proliferation. In addition, there are two structural proteins that are expressed last, namely the late genes L1 and L2, which play a role in the formation of the viral capsule.

The International Committee on the Taxonomy of Viruses classifies Papillomaviruses into the family Papillomaviridae. Previously, Papillomavirus and Poliovirus belonged to the same family. The family Papillomaviridae is divided into two subfamilies and includes more than 50 genera. In the context of infection in humans, there are five relevant genera, with a total of about 225 types of HPV grouped into five categories, namely alphapapillomavirus (α), betapapillomavirus (ß), gammapapillomavirus (γ), mupapillomavirus (μ), and nupapillomavirus (ν). Among these genera, the genus alphapapillomavirus is the most common found in humans. A subgroup of about 15 types of HR-HPV α can cause invasive carcinoma, including HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. HPV 16 is found in 50% of cervical cancer cases worldwide, while HPV 18 is found in about 14%. However, in Indonesia, HPV 18 is more frequent (49%) compared to HPV 16 (32%) in cases of diseases caused by the HPV genotype [4]

Human papillomavirus (HPV) is the main cause of the risk of cervical cancer. The process of developing cervical cancer is strongly related to metaplasia, which can be triggered by mutagens, generally derived from sexually transmitted agents, such as HPV. This process begins when HPV enters as an initiator of cell disorders in the cervix (Rasjidi, 2010). HPV types 16 and 18 are responsible for about 70% of cervical cancer cases. Cervical cancer is the second highest type of cancer in Indonesia. In 2018, it is estimated that the incidence of cervical cancer in Indonesia reached 23.4 per 100,000 women, with a mortality rate of 13.9 per 100,000 women (IARC, 2019). In DKI Jakarta province, cervical cancer also ranked second highest in 2012 with an incidence of 9.25 per 100,000 women (Wahidin et al., 2012). In 2017, HPV vaccination

coverage for grade 5 elementary school in DKI Jakarta reached 89.4%, and in Central Jakarta it was 90.1%. [5]

HPV vaccination in adolescents is one of the main steps in the prevention of cervical cancer. Since 2009, the World Health Organization (WHO) has recommended that HPV vaccination be included in the national immunization program in every country. The most ideal age to receive vaccination is between 9 to 14 years old, which is before women start sexual intercourse (WHO, 2006). The recommended HPV vaccine is at least a bivalent HPV vaccine (types 16 and 18), and even better if the vaccine includes more than bivalent to protect against HPV type 52. [5]

The Indonesian government has been implementing an HPV vaccination program to overcome cervical cancer since 2016. HPV vaccination began in DKI Jakarta and continued gradually to other regions in Indonesia until now. In 2017, vaccination was carried out in DI Yogyakarta; in 2018, in Surabaya; in 2019, in Manado and Makassar; in 2020, in Karanganyar and Sukoharjo Regencies; in 2021, in Kediri and Lamongan; in 2022, in Bali, East Java, and Central Java; And in 2023-2024, vaccination is planned to be implemented nationally. [6]

The HPV vaccine is available in three types: bivalent, quadrivalent, and nonavalent. The quadrivalent vaccine protects against four types of HPV (6, 11, 16, and 18), while bivalent protects against types 16 and 18. The nonavalent vaccine protects against five additional types (31, 33, 45, 52, and 58). All vaccines are administered intramuscularly, and clinical trials in young women (15-26 years) show a good immunogenicity profile. Although there are no efficacy studies in target adolescents, studies show a strong immune response and good safety. The HPV type 16/18 vaccine can prevent about 66.2% of cervical cancer cases. [7]

The factors that affect the effectiveness of HPV immunization program management in cervical cancer prevention: [8]

1. Human Resources
2. Funding
3. Facilities and Infrastructure
4. Planning and Pre-implementation
5. Distribution and Implementation of Immunization
6. Monitoring and Evaluation
7. Immunization Program Acceptance

8. Sustainability Efforts

According to Williams Gynecology (2016), the high-risk HPV vaccine can reduce the incidence of cervical cancer by up to 90%. However, the vaccine is only effective in preventing HPV infection after administration and cannot protect against previously infected cervical cancer. Overall, the HPV vaccine is very effective in reducing the risk of cervical cancer and is the right solution for prevention in women. However, concerns about side effects that may arise after HPV vaccination remain.

The possible side effects of the HPV vaccine are generally mild, and serious side effects have been ruled out based on observations made in many patients who have received the vaccine before. Thus, women who will receive the HPV vaccine as a preventive measure for cervical cancer can feel safer. In addition, it is important to discuss government programs and policies related to the HPV vaccine so that it can be widely accepted by the public.

The Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) has developed recommendations regarding all vaccinations in the United States, including HPV vaccination. The current ACIP recommendations for HPV vaccination are:

1. Children and adults aged 9 to 26 years.
2. Adults aged 27 to 45 years.
3. People who are pregnant

The HPV vaccine guidelines for women from the Indonesian Association of Internal Medicine Specialists in 2017 stated that the HPV vaccine available in Indonesia is bivalent or quadrivalent. Maximum vaccine effectiveness is obtained if given to women aged 9 to 26 years or who are not sexually active. The maximum age of vaccine recipients is up to 55 years old. Even though vaccination is carried out, early detection such as Pap smear or IVA still needs to be done at least every 3 years. In addition, pregnant women in Indonesia are not recommended to receive the HPV vaccine and are advised to wait until the pregnancy or birth process is complete.

The HPV vaccination program has proven to be effective in preventing cervical cancer in Indonesia, as seen from the reduction in incidence rate by up to 90%. Vaccination can protect against HPV infection that occurs after vaccination, but it cannot prevent pre-existing cervical cancer. Studies show that women who receive one dose of the vaccine are less likely to develop abnormal cervical cytology. HPV vaccination can reduce the incidence of cervical cancer by 86%

and 68% in girls vaccinated before the age of 16 or between 17-19 years. Women who were vaccinated before the age of 17 had an 88% lower chance of developing cervical cancer than those who were not vaccinated. The effectiveness of HPV vaccination will be more optimal if done from an early age, because women over 20 years old may have been exposed to HPV before getting the vaccine.

Conclusion

HPV vaccination has been shown to be effective in preventing cervical cancer, especially in preventing infections caused by high-risk HPV types such as types 16 and 18, which are responsible for about 70% of cervical cancer cases. The HPV vaccination program in Indonesia has been implemented in stages since 2016, with the main target being women aged 9 to 14 years, according to WHO recommendations.

Although the program has been successful in some regions, there are challenges such as socioeconomic factors, vaccine myths, and parental rejection, which hinder optimal vaccination coverage. Therefore, public education is very important to increase understanding of the benefits of the HPV vaccine and overcome these barriers.

References

1. Faisal M, Dhuha A, Irawan MP, Juwita S, Wulandini P. Cervical Cancer Education and the Effectiveness of HPV Vaccine Early at SMAN 2 Pekanbaru. Journal of Health Service (JAK) 2022; 4(2):329.
2. Nita V, Novi Indrayani. Health Education in an Effort to Prevent Cervical Cancer in Women of Childbearing Age. Dynamisia: Journal of Community Service 2020; 4(2):306–310.
3. Samaria D, Desmawati D, Marcelina LA, Dwinova R, Mawaddah F, Mizka NZ. Health Education on Human Papilloma Virus Vaccination to Prevent Cervical Cancer in Female Students in East Jakarta. Journal of Community Service Creativity (PKM) 2023; 6(7):2916–2930.
4. Sono RH, Dewi R, Sari P, et al. Effectiveness of Human Papillomavirus Vaccine in Girls in Cervical Cancer Prevention Efforts.

5. Wahidin M, Febrianti R. Overview of the Implementation of the Human Papilloma Virus (HPV) Vaccination Program in Two Health Centers in Central Jakarta City in 2020. Health Systems Research Bulletin 2021; 24(3):182–191.
6. Zakiyah H. Effectiveness of the HPV Vaccination Program in Preventing the Incidence of Cervical Cancer in Women in Indonesia [Homepage on the Internet]. Available from: https://www.researchgate.net/publication/376642104
7. Suryoadji KA, Ridwan AS, Kusuma F. HPV VACCINE AS A CERVICAL CANCER PREVENTION STRATEGY IN INDONESIA. JIMKI : Scientific Journal of Indonesian Medical Students | 2022;10.
8. Sono RH, Dewi R, Sari P, Lisiswanti R, Romulya AI. Factors Affecting the Effectiveness of HPV Immunization Program Management in Cervical Cancer Prevention. Action Research Literate [homepage on the Internet] 2024; 8(4). Available from: https://arl.ridwaninstitute.co.id/index.php/arl