International Journal of Community Medicine and Public Health
Sharma M et al. Int J Community Med Public Health. 2024 Nov;11(11):4554-4558
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20243322

Review Article

Human papillomavirus vaccine for cervical cancer prevention in India: new improvement and way forward

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Received: 21 August 2024
Accepted: 06 October 2024

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ABSTRACT

Cervical cancer is the malignant abnormal changes in the tissues of cervix mostly transmitted through the human papilloma virus. Prophylactic vaccination against HPV is effective strategy to prevent cervical cancer. India has access to two types of vaccines that are licensed worldwide, the bivalent cervarix and the quadrivalent Gardasil. The drug controller general of India has authorized "CERVAVAC" a new HPV vaccination that is less expensive and is being offered in India as a single dose for females between the ages of 9 and 19 years. The government said in February 2024 that girls between the ages of 9 and 14 will receive the HPV vaccine as part of universal immunization programme. There are significant obstacles to vaccination implementation in India like lack of epidemiological evidences for illness prioritization, vaccine duration, parental attitude and vaccine acceptance. The WHO's goal of eradicating cervical cancer by 2030 depends on implementing socially and culturally relevant public awareness campaigns after educational initiatives for healthcare professionals.

Keywords: Cervical cancer, Cervarix, Cervavac, Gardasil, Human papilloma virus

INTRODUCTION

Cervical cancer is the malignant abnormal changes in the tissues of cervix mostly transmitted through the human papilloma virus. If found and diagnosed early enough and treated appropriately, cervical cancer is one of the most treatable and preventable type of cancer.[1] HPV infection is commonly transmitted through sexual contact and also disturbs skin, throat and genital area. Most persons who engage in sexual activity will get infected at some points in their lives but usually without appearance of any sign and symptom as defense mechanism of body rid of body from HPV virus. In few cases high risk HPV infection can persist for longer period which can lead to the development of aberrant cells that eventually turn into cancer.[2] Estimated to be fourth most frequent disease in women worldwide, cervical cancer will cause 342000 deaths and 604000 new cases in 2020. According to GLOBOCAN 2020, cervical cancer is second most prevalent cause of death in India, accounting for 9.1% of all deaths and third most common type of cancer overall, with an incidence rate of 18.3% (123,907 cases). In India, 6-29% of all malignancies in women were cervical cancer.[3]

95% of cervical cancer are caused by untreated persistent HPV infection of the cervix. The most prevalent cancer-causing types, 16 and 18, account for 70% of all reported cases of cervical cancer and 63% of high-grade lesions. Precursor lesion caused by HPV often take 10 to 20 years to progress into aggressive malignancy.[4] Squamous cell carcinoma makes up the majority of cervical cancers up to 90% of cases. The exocervix is the source of these tumor cell. The junction of the glandular and squamous cell areas is known as the transformational zone where squamous cell carcinomas start. Other cervical cancers

are adenocarcinoma which develop from glandular cells.[5] The risk factors for progressive cervical cancer are early initiation of sexual activity, grade of oncogenicity of the HPV Type, female with higher parity, use of hormonal contraceptives, presence of other sexually transmitted diseases, age at first pregnancy, multiple sexual partners and smoking.[6] In early stages, cervical cancer may not exhibit any signs and symptoms. Bleeding between regular periods and bleeding after sex may be symptoms of advanced cervical cancer.[7]

In order to meet world health organization's 2030 deadline for eliminating cervical cancer, a targeted approach is necessary. The world health assembly formally unveiled a global implementation strategy on 17 November, 2020 which is 90% of girls receive two doses of the HPV vaccine by the time they are 15 years old, 70% of women are screened with a high performance test between the ages of 35 and 45 and 90% of women who have cervical pre-cancer and cancer receive treatment to reduce the number of cases per 100,000 women to less than four.[8] The HPV vaccine, regular cervical cancer screening and adequate follow up care, when necessary, could prevent almost all cervical malignancies. A concerned effort is needed to increase women's knowledge of primary and secondary prevention techniques, as well as their access to care for treatment and palliation, in order to prevent and control it.[9]

CERVICAL CANCER VACCINATION

Why vaccination is best method of prevention?

As of right now, the only ways to avoid genital HPV infections are lifetime mutual monogamy and abstinence. There is insufficient proof to suggest that barrier contraceptive techniques, usage of condoms, in particular, offers protection against HPV infection. Secondly the infection is asymptomatic, with the exception of genital warts. Even in the developed nations, the vulnerable female population adherence to routine screening with periodic pap smear has not been sufficient; In contrast, large scale routine screening is challenging to achieve in developing nations like India.[10,11]

There are six HPV vaccination in the market as of 2023 which are three bivalent, two quadrivalent and one nonavalent. All has been demonstrated to be safe and effective in preventing HPV infection and cervical cancer. They offer protection against the high-risk HPV strains 16 and 18, which are responsible for the majority of cervical malignancies.[1]

Type of vaccine

India has access to two types of vaccines that are licensed worldwide. The bivalent cervarix(marked by Glaxo smith kline) and the quadrivalent Gardasil (marketed by Merck). Both vaccinations are highly safe; they are created using very little bits of the human papilloma virus that cannot infect people. Both vaccines are licensed, safe and effective for females ages from 9 to 26 years.[12]

Bivalent vaccine (Cervarix)

HPV types 16 and 18 are included in this vaccination.

Quadrivalent vaccine (Gardasil)

HPV type 6, 11, 16 and 18 are included in this vaccine. Gardasil protect against HPV types 6 and 11, which are responsible for the majority of genital warts in both men and women. It also shown protection against anus, vaginal and vulval malignancies.

Nona valent (HPV 9)

HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 are included in this vaccine. In India, it is anticipated that the nonavalent vaccination (HPV 9) will prevent approximately 98% of cervical cancers, while the bivalent and quadrivalent HPV vaccines will prevent about 83% of cervical cancers.[13,14]

Schedule of vaccine

Girls aged 9 to 14: Two doses should be given at an interval of six months with regimen of 0-6 months, either of HPV4 (Gardasil) and HPV2 vaccine (cervarix). For girls aged 15 and above: the schedule suggests three doses. 0-1-6 months for cervarix and 0-2-6 months for Gardasil.[15] For immunocompromised people of any age, three doses of cervarix (0-1-6 months) and Gardasil (0-2-4) are advised according to the schedule. HPV 9 is authorized for use in boys 9-15 years old and females 9-26 years old in a 3-dose regimen of 0-2-6 months. 9-10 years old is the optimal age to begin the vaccination. In India only the HPV 9 vaccine is licensed in males.[16]

Why it is imperative that the schedule begin at age 9-10 years and not later?

It is imperative to receive all doses of the HPV vaccination prior to HPV exposure in order for it to function as intended. The first time someone has intercourse with another individual, they may be infected with HPV. When compared to older adults, young adolescents exhibit a stronger immunological response. Early illness prevention is preferable to later prevention. In this age range, just two doses are required, however after the age of fifteen, three doses are required. It is not advised to take any booster dosage.[17]

Are vaccinations against HPV are safe?

In general, these vaccinations ae safe. Pain edema or redness at the vaccination site are examples of mild to moderate local side effects.

Certain teenagers may experience vertigo or feeling of fainting following the injection. By administering the vaccination while reclining or on your side, it might be reduced. For at least twenty minutes every patient should be watched for any adverse effects that could arise.[10]

Who should not receive the HPV vaccine?

History of severe allergic reaction (anaphylaxis) after the first dose of the vaccine or known, sever allergies to any component of vaccine. It is not recommended that pregnant women receive the vaccination. Pregnancy termination is not acceptable based on receiving the HPV vaccination while pregnant. However, a pregnant woman should wait to receive any doses of either HPV vaccination until her pregnancy is over in order to be safe. People who are moderately or severely ill should usually wait until they recover, before getting HPV vaccine.[10]

WHO New recommendation

The WHO has revised its recommendations for the human papilloma virus vaccination in new position paper. The position paper came in the matter of gravely alarming global drop in HPV vaccine coverage. Coverage of the first dose of HPV vaccination decreased from 25% to 15% between 2019 to 2021. This indicates that, in comparison to 2019, 3.5 million more girls were not vaccinated against HPV in 2021.[18]

The study makes special notice of the claim that a single-dose schedule, also known as an alternate, off-label single dose schedule, can offer protection that is just as effective and long lasting as a two-dose regimen. WHO's independent expert advisory panel, SAGE (Strategic Advisory Group of Experts), first recommended alternate single dose schedule in April 2022.[19]

WHO now recommends

A single or double dosage schedule for girls aged from 9-14 years. A single or double dosage schedule for girls and women aged 15-20 years. Provide double dosage separated by six months interval for women older than 21 years. Individuals with impaired immune system have to get a minimum of two doses, and if feasible, three doses.[20]

It is anticipated that the HPV schedule optimization would enhance vaccine accessibility, providing nations with the chance to increase the number of girls who can receive the immunization and lessen the strain of the sometimes difficult and expensive follow-up necessary to finish the vaccination series. Countries must bolster their HPV vaccine programs, move quickly to adopt them, and reverse the decline in coverage. Over the next 100 years, it is predicted that putting this method into practice might avert 45 million deaths and 60 million instances of cervical cancer.[21]

Cervavac

India has introduced cervavac the first domestically made version of the human papilloma virus vaccine marking a hopeful step forward in the country's fight against cancer. It is a quadrivalent vaccine. It targets HPV-6, 11, 16 and 18 strains of the human papillomavirus. Since January 2023, this is the first domestic vaccine made in India that is offered for sale. A more accessible and reasonably priced vaccination, India's first indigenous HPV vaccine has the potential to transform the game.[22] The drug controller general of India has authorized " CERVAVAC" a new HPV vaccination that is less expensive and is being offered in India as a single dose for females between the ages of 9 and 19 years.[23] Immune system of our body is prompted by the cervavac vaccine to create antibodies that neutralize the virus and stop it from entering your cells and causing illness. Like other cervical cancer vaccinations, slight soreness, redness or swelling at the injection site are common adverse effects. Serious adverse effects are uncommon.

In the battle against cervical cancer, the launch of cervavac- india first HPV vaccine-marks a critical turning point. With the help of this revolutionary vaccination, the incidence of cervical cancer in the nation may be decreased and HPV infection can be prevented. Cervavac has the potential to save many lives and enhance the general health and wellbeing of people and communities because to its great effectiveness, safety and accessibility.[24]

Indian government initiative to promote HPV vaccine

The government said in February 2024 that girls between the ages of 9 and 14 will receive the HPV vaccine as part of universal immunization programme. This is a big step toward making the vaccine more widely available and reasonably priced. As part of the universal immunization programme expansion, funding was allotted in the 2024 interim budget for the acquisition and distribution of HPV vaccinations. The government intends to immunize a substantial number of girls in the target age range against HPV by holding vaccination programs in school.[25] Communities are being educated about HPV infection, cervical cancer, and the advantages of vaccination through a variety of outlets, including as local media, Anganwadi centers and ASHA employees. To increase accessibility and convenience, vaccination registration and information are being made available via digital channels. The government is working with regional, national and international health agencies like as UNICEF and WHO to provide technical support for the development, execution and oversight of the HPV vaccine campaign.[26]

NGOs are essential in tackling vaccine reluctance, energizing communities, and raising awareness of early diagnosis and screening for cervical cancer. Research institutes and pharmaceutical corporations are working

together to create new screening techniques, increase access to therapy, and lower the cost of vaccines.[27]

Challenges and future directions

Although the government efforts are praiseworthy, obstacles still need to be overcome to guarantee that everyone in the socioeconomic and geographic categories has fair access to vaccination. While we support these activities, we also need to recognize that there are still issues to be resolved, such guaranteeing equal access, addressing vaccination hesitancy, and doing ongoing research to optimize programs.

In addition to potentially saving countless lives, India has the ability to establish a precedent for successful public health initiatives by working together to address these issues and build on the momentum that is now present. Combating cervical cancer is not only a medical endeavor; it is also a national responsibility to the welfare of women and their families. It is important to teach young girls, who are mostly under the age of 15, about the cervical cancer vaccine. This may be done by making the sexual health a more prominent topic in the curriculum or by training parents on how to best communicate with their children about sexual health. India can clear the path for a healthy future free from shadows produced by these silent and fatal diseases by continuing its devotion and working together.[25,28]

CONCLUSION

In the battle against cervical cancer, the launch of cervavac-India's first HPV vaccine-marks a critical turning point. Even with this chance, it is still unlikely that HPV and cervical cancer will be completely eradicated in India by 2030 or later due to a host of problems, including parental attitudes, vaccine acceptance, myths, misinformation, lack of awareness, lack of well-organized screening program, a shortage of trained personnel and access to effective treatment. It won't be effective until the Indian government takes the proactive steps of making this vaccination required through National immunization program for both boys and girls. The WHO's goal of eradicating cervical cancer by 2030 depends on implementing socially and culturally relevant public awareness campaigns after educational initiatives for healthcare professionals.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Sharma M, Kaur E, Sandhu R, Kaur S. Human papillomavirus vaccine for cervical cancer prevention in India: new improvement and way forward. Int J Community Med Public Health 2024;11:4554-8.