

Human Papilloma Virus Vaccine- Development and perception in India (A Review Study)

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ABSTRACT

HPV is a serious public health issues, as it is responsible for the overall incidences of cervical cancer. High risk papilloma virus (HPV) type 16 and 18 has been proven as central causes of cervical cancer. The main mode of HPV transmission is sexual contact. HPV vaccine is considered as one of the most effective practices against HPV. Safety and immunogenicity of HPV vaccine are sufficiently established. The international literature has demonstrated that HPV vaccination programme can reduce the burden of disease associated with HPV, such as cervical cancer.

However the wide acceptance of HPV vaccine by the people is yet to be achieved in spite of the supporting literature about the effectiveness and safety. Lower knowledge level and less confidence in safety and efficacy of the vaccine can negatively affect the intention to get vaccinated. Most people have the perception that the vaccine is expensive. Indian people also have low perception of contracting HPV infection especially when it comes to vaccinating their adolescent kids of HPV, which is contracted by sexual encounters (not an acceptable risk by parents). Lack of government policies and concrete recommendation from healthcare provider also have a negative impact when it comes to vaccinate against HPV.

The most common factors which affects the decision making process of parents or women are lack of knowledge, cost of vaccination, efficacy of vaccination, safety of vaccination and provision of information on vaccination.

Keywords: cervical cancer, human papilloma virus, vaccine, perception, adolescent.

INTRODUCTION

Cervical cancer is a type of cancer that develops in the cells of cervix- the lowermost part of uterus (1). According to ranking, cervical cancer is the most frequently occurring cancer in women in India. 365.71 million Women in Indian population are above 15 years of age and this age group is at highest risk of developing cervical cancer. India accounts for a nearly one third cervical cancer deaths, occurring globally among which 2.5% of Indian women faces a lifetime risk of getting cervical cancer and 1.4% women are at cumulative risk of death caused by cervical cancer. It is estimated that, at any given point of time, 6.6% women among the general population are at higher risk of harboring cervical infection caused by Human Papilloma Virus. (2)

Cervical cancer, mainly caused by human papilloma virus (HPV), is the leading cancer in Indian women and the second most common cancer in women worldwide. (3)

HUMAN PAPILOMA VIRUS

More Than 30 strains of the human papilloma virus (HPV) can affect a person's genitals. (4) HPV Types falls into two groups' low risk and high risk. Low risk HPV's mostly cause no disease. However, a few of the low-risk HPV types can cause warts on or around the genitals, anus, mouth or throat. Most severe type of cancers is caused by High risk human papilloma virus. There are about 14 high risk HPV types including HPV 16,18,31,33,35,39,45,51,52,56,58,59,66,68.

Two of these, HPV 16 and 18 are responsible for most HPV related cancers. (5)

HPV is the most common sexually transmitted infection. It is passed from one person to another during sexual activity. (6) About 30 HPV strains can affect the genitals of the infected person, including vulva, vagina, cervix, penis and scrotum as well as rectum and anus. (4). HPV can infect anyone regardless of their sex, gender identity or sexual orientation. (5)

SYMPTOMS OF HPV INFECTION

1. Genital warts: - Small cauliflower like bumps or tiny stem like protrusions appears. In women, genital warts mostly appear on the vulva, anus, cervix and sometimes vagina.
2. Common warts: - They are rough, raised bumps that appear on hands and fingers. These warts can be sometimes painful and may be susceptible to injury which can lead to bleeding.
3. Planter warts: - They are hard, grainy growth that usually appears on the heels or balls of your feet.
4. Flat warts: - They are flat-topped, slightly raised lesions which can appear anywhere. (7)

PREVENTION OF HPV INFECTION

The only way and unattainable way to prevent HPV is to abstain from any form of sex. The main preventive measure which can prevent and control the spread of HPV are as follows: -

1. HPV Vaccine: - vaccination is the best way to get vaccinated before becoming sexually active. There are certain vaccines available in market which are produced internationally and indigenously both. (4) HPV vaccinations work exactly like other immunizations that guard individuals against viral infections. It stimulates the production of antibodies in the future, the virus is prevented from infecting the cell. (8)
2. Get screened and tested regularly: - Early detection of HPV and abnormal

cells prevent cervical cancer. A sexually active woman should start getting screened (PAP smear) at the age of 21 and then according to need and requirement getting it done every one to three year. Between the ages of 30 to 65, routine Pap smear should be done and after 65 years of age it may or may not be required.

3. Practice safe sex: - Condoms are less effective at preventing HPV than protecting against STI's that spread through the risk of HPV infection.
4. Protect your partner(s) : - If a person is having HPV, He/she should inform their partner about the same, so that they can get tested too. (4)

HUMAN PAPILOMA VIRUS VACCINATION

HPV vaccine protects against infection with human papilloma virus (HPV). HPV vaccines currently in use are based on virus like particles (VLP). All the vaccines are made by using HPV surface components, but due to the lack of HPV's DNA, they do not cause HPV infection. The VLPs used in vaccines promotes the production of antibodies in large number inside the body, this makes the vaccine highly effective. The HPV vaccine, however, doesn't prevent other sexually transmitted diseases or cure existing HPV infections or HPV caused diseases. (8) as shown by many trials which were conducted to test the efficacy of HPV vaccine, it is found that HPV vaccines have an efficacy of nearly 100% in preventing cervical cancer, which are caused by Human Papilloma Virus of higher risk group. (1) The HPV Vaccine is recommended because

- One out of four women dies of cervical cancer in India.
- Annually 67,477 Indian women dies due to cervical cancer.
- Every seven minute one women dies of cervical cancer in India.
- Human Papilloma Virus (HPV) has been detected in 99.7% of all cases of cervical cancers worldwide.

- This is the highest levels of the associated pathogen known to be a major cause for a human form of cancer.
- HPV types 16 and 18 are responsible for 82% cervical cancer in India.(6)

In an effect to combat the incidences of cervical cancer in India, the government has announced plans to administer the human papilloma virus vaccine to girls aged nine to fourteen years in 6 states.(9)

In January 2023, The Indian Ministry of Health and Family Welfare wrote to seven state governments from Himachal Pradesh to Tamil Nadu requesting them to start preparations for the roll-out of the human papilloma virus vaccine for girls aged 9-14 years. Once the notified states have covered children aged 9-14 years, HPV vaccine will become part of their routine immunization programme. (10)

This step was taken after Serum Institute of India has developed India's first indigenously developed vaccine to prevent cervical cancer, CERVAVAC, which was launched on 24th January 2023. This vaccine will be available at the cost of Rs 2000 per Pre filled single shot vial. (1)

Similar efforts will follow in another set of status and union territories in 2024 and again 2025.68 million girls in India have been targeted to get vaccinated against HPV by the end of the second phase of vaccination programme. A further 11.2 million girls aged 9 years will subsequently be targeted for routine HPV vaccination each year. (10)

HISTORY OF HPV VACCINE DEVELOPMENT

In 1980's, work started in the field of developing vaccine for HPV, once it was identified as the primary cause of cervical cancer. In the 1980's and 1990's, studies in animal models demonstrated that animal could be protected against papilloma virus lesions using purified virions, that neutralizing antibody was necessary and sufficient for the protection against viral challenge and that protection was likely specific to HPV type.

GlaxoSmithKline Biologicals (GSK) and Merck & Co. GSK are the two USA based companies, which started the initial commercial development of HPV vaccine. GlaxoSmithKline Biologicals (GSK) developed a bivalent vaccine (Cervavax) composed of HPV-16 and HPV-18 VLP's. Merck developed a quadrivalent vaccine (Gardasil) with HPV-16 and HPV-18 as well as HPV-6 and HPV-11 VLP's. Ceravax was approved in 2007 and Gardasil 9 was approved in 2014. (11)

WHO SHOULD GET HPV VACCINE

HPV vaccination is recommended at age 11-12 years. 9 years is the starting age to give HPV vaccine to the adolescent girls. According to CDC, U.S.A., the first dose is routinely recommended at ages 11-12 years old. If the first dose was given before 15th birthday, later only two doses are required. Children age 9 through 14 years who have received two doses of HPV vaccine less than 5 months apart will need a third dose. Three doses are also recommended for people aged 9 through 26 years who have weakened immune system. (12)

In India HPV vaccination is recommended for all sexually active adults. In India it can be given until age 45. But the best time is between 9-13 years of age before they become sexually active. Once a woman become sexually active she may be exposed to one or more strains of HPV and although vaccinations can be still taken, it may not guaranty protection if the woman is already infected with HPV 16 or HPV 18. (6)

WHO SHOULD NOT GET HPV VACCINE

The people who should not get HPV vaccine are

- Anyone who has ever has a life threatening allergic reaction to any ingredients of an HPV vaccine or to a previous dose of HPV vaccine.
- Those who have allergy to yeast (Gardasil and Gardasil 9)
- Pregnant women.(12)

HEALTH RISK OR SIDE EFFECTS OF HPV VACCINE

Many studies have been conducted so far to assess the risk and benefit ratio. Jorgensen, Gotzsche and Jefferson (2020) conducted a meta analysis study to assess the benefits of the human papilloma virus (HPV) vaccine. After studying 24 studies (out of 50 eligible studies), for a period of 4 years, they concluded that the extent to which HPV vaccine benefits outweighs their harm is unclear. (13)

Also, Ana, Cobucci, Rodrigues et al (2014) conducted a review study on safety, tolerability and side effects of human papilloma virus vaccine. Twelve reports of HPV vaccine safety and adverse effects involving 29,540 subjects were included. The results show that most of the patients who received HPV vaccine have reported injection site reaction. Headache and fatigue were the most common vaccine related systemic adverse reaction seen in approximately 50-60% of all participants. Fatigue was the most relevant general effects observed followed by fever, gastrointestinal symptoms and headache. (14)

The documented side effects of HPV vaccines are

1. Injection site pain
2. Swelling and redness at vaccination administration site.
3. Mild fever.
4. Sometimes dizziness or fainting occurs after the injection.
5. Other adverse effects include- headache, nausea, vomiting, fatigue or weakness.

PERCEPTION, KNOWLEDGE AND BARRIERS REGARDING HPV VACCINE

CERVAVAC is the first indigenously developed vaccine in India which was launched in Jan 2023. But the problem we faced in HPV vaccination is not only the unavailability of vaccine but the knowledge regarding the same. In India people are not aware of the availability of the vaccine for cervical cancer. HPV vaccination coverage

is lower among the Indian population because of lack of awareness about HPV, the absence of proper screening programmes, lack of availability of vaccine and its high cost.

Various studies which were conducted to study the level of knowledge among adolescent girls, showed that the average level of knowledge regarding cervical cancer was not adequate (15, 16) and they have poor level of knowledge regarding HPV vaccine (17, 18).

It's not just adolescent girls or their parents, but the health care workers, especially nursing students and staffs, also the ones who possess less knowledge regarding the cervical cancer and vaccine availability and those who have some knowledge regarding the same, do not perceive getting vaccinated against HPV as important. (18, 19)

Even after more than 15 years of laborious research and evidence which proves that HPV vaccine is safe and effective, some studies have shown that in recent years more parents are showing concern about the safety of available vaccine. Some parents have always cited concerns about safety for declining to get the HPV vaccine for their kids. But from 2015 to 2018, the study showed the percentage of parents who decline the HPV vaccine for their kids due to safety concerns nearly doubled. (20)

Studies conducted in different parts of the world shows that education on HPV infection and vaccination plays a critical role in HPV Vaccination uptake. It is found that the higher age and educational levels of people correlates directly with their increased knowledge related to the HPV infection and its complication.

Medical professionals including doctors and nurses are the main resource person who held high stakes in scaling up the HPV vaccination, because being from the field of medicine, their suggestions and recommendations will play a crucial role in decision making by the people. Doctors and patients' communication is a modifiable factor which can impact the uptake of HPV vaccination. Some studies have been

conducted to assess the knowledge and attitude of doctors' pertaining to human papilloma virus vaccination in India. (21) These studies concluded following points regarding perception and awareness of HPV vaccine among the people through the point of view of doctors: -

- Most of the doctors believed that cervical cancer can be prevented effectively through raising awareness, screening and HPV vaccination. However they felt that it needs to be a priority for the government- as there is currently not strong political commitment or attention in country's maternal and child health programmes given to cervical cancer and HPV vaccination.
- Lack of awareness about cervical cancer among patients and in the community is main reason for lagging behind in HPV vaccination (and also screening of cervical cancer). Even the lack of awareness among the physician serving in rural community is also one of the reasons.
- Majority of doctors believed that HPV vaccination is necessary and effective in preventing cervical cancer. However some did not think it was necessary to give to adolescent girls and there were apprehensions related to the vaccines effectiveness after sexual debute in older ages.
- Some doctors do not believe in burdening their patients with additional information apart from the current health concern and also they do not recommend HPV vaccines to male adolescent because they think that it only prevents female diseases.
- As mentioned earlier about the side effects of vaccination, most of the doctors also mentioned general side effects associated with HPV vaccination such as pain in the injected site, redness, inflammation and fever. However, some doctors believed them to be common side effect for all vaccines.

There are various factors which affect the individual's intention to decide to whether get vaccinated or not. In most of the cases having knowledge and getting vaccinated are not associated with each other. In many studies the women have knowledge about HPV virus and its vaccine but still choose not to get vaccinated. Most of the women in India do not give much priority to their own health and neglect it as they do not have time to think about themselves. When they come to hospital they have already reached the advanced stage of cervical cancer. The chances of getting vaccinated are higher among women who perceive themselves at risk of contracting the virus, in comparison to those who do not. Some women still don't see themselves as being high risk of getting HPV or cervical cancer. (21) The person who has some kind of exposure to cervical cancer in person or the relative or those who perceived the seriousness of this disease, have a higher chance of getting vaccinated whereas others might not. As stated earlier many people are hesitant to take vaccine because of the side effects of HPV vaccine. (20) Mainly female parents and young women are more concerned about the side effects of vaccine. Some people have concern about the cost and efficacy of the vaccine. As total cost of three doses of one vaccine is higher, this is difficult for everyone to afford. (21)

CONCLUSION

Cervical cancer is the only cancer among women, which can be prevented, if women undergo regular screening and if adolescent girls (and unvaccinated women) are vaccinated. But because of lack of information and knowledge among the general population the acceptance and perception regarding HPV vaccine is very low. Various studies show that the adolescent girls do not have adequate knowledge regarding cervical cancer and its preventive measures. The nursing students, nursing staff and rural physicians (mostly) do not possess enough knowledge regarding the HPV vaccine. With the launch of

indigenous HPV vaccine in India, now the availability of this vaccine has been put in notice. The government of India has launched a vaccination programme for its administration among 9-12 years adolescent kids. Soon it will be included with National Immunization Programme.

But the main issue with HPV vaccination is not the availability or unavailability of vaccine but it is the intention, acceptability and willingness of people to have HPV vaccine. Concerns of parents (especially mothers) regarding the efficacy, effects and side-effects of HPV vaccine is also a prime factor for not planning to take HPV vaccine. In Indian scenario another important reason for not taking HPV vaccine is the influence of others such as parents, husband or partners on women's decision to have HPV vaccine.

Declaration by Authors

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