

Current Trends and Future Prospective of Human Papillomavirus Vaccination - Need, Impact, and Challenges

Abstract

Human papillomavirus (HPV) is a group of viruses that commonly produce skin or mucous membrane growths. It is most often transmitted through the sexual route and is a common etiological factor for as many as six types of cancers, but majorly, the cervical cancer; implying the impact of cervical cancer worldwide could be reduced by widespread immunization with the HPV vaccine. The HPV vaccine, in two separate doses, can be given starting from 9 years of age, and is highly recommended for females of (or entering) the sexually active age group; it is considered to be very safe and effective, as reported after 12 years of monitoring and research. Although HPV vaccination is the approved public health intervention to reduce the risk of developing HPV-associated cancers, it is yet to see a large-scale implementation. In this article, we discuss about the vaccine, its benefits, the reasons regarding its unacceptance, and whether it is merely an adjunct preventive measure or a necessary one.

Keywords: Cervical cancer, human papillomavirus, oropharyngeal cancers, vaccination, vaccine

Introduction

India contributes to 25% of deaths due to cervical cancer worldwide; not surprising considering that >122,000 women are diagnosed with cervical cancer every year, out of which >67,000 die, making it the second leading cause of cancer deaths in India and therefore a major concern of public health. The most common cause of cervical cancer is the human papillomavirus (HPV): A group of relatively small, double-stranded DNA viruses that replicate their genome by utilizing host machinery, leading to the deregulation of the hosts genomic expression, and subsequently, the formation of abnormal growths. As of now, there over hundreds of strains identified, of which about 15 are implicated in the causation of cervical cancer, of which HPV-16 followed by HPV-18 are the most oncogenic.^[1,2]

More than 20% of all cancers in India are attributed to HPV and though the burden of HPV is undisputedly felt heavily through cervical cancer, it is also known to cause oropharyngeal and anogenital cancers, though the prevalence shows great discrepancy.^[1] A recent investigation into an

epidemic increase in oropharyngeal cancers, especially that of the tonsil and base of the tongue, in Western countries, where the incidence of smoking had been on a declining trend (ruling out its importance as an etiological factor), pointed fingers toward HPV. The above incidence drew up a call for the vaccination of males too, as 80%–90% of the oropharyngeal squamous cell carcinomas were from HPV-16, a vaccine-preventable strain^[3]

Human Papillomavirus Vaccine

Currently, there are three licensed prophylactic HPV vaccines available: (i) Gardasil: A quadrivalent vaccine against HPV type 6, 11, 16, and 18; (ii) Gardasil 9: A nonavalent HPV vaccine targeting HPV type 6, 11, 16, 18, 31, 33, 45, 52, and 58; and (iii) Cervarix: A bivalent HPV vaccine against 16 and 18. As stated above the most oncogenic serotypes of the virus are 16 and 16, followed by 6 and 11. The serotypes 31, 33, 45, 52, and 48 are of less oncogenic power, however, these are of no less importance, considering, for example, HPV 33 which is second in etiology of oropharyngeal cancer and third in cervical, vulvar, and anal cancers.^[2]

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Vaccine Efficacy Merits and Demerits

The European public assessment report for Gardasil conducted a study on 16,947 girls (uninfected by HPV), who were randomly split into two groups; one group of 8487 received the vaccine, whereas the other 8460 girls received a placebo. On follow-up after 2 years, none of the girls who received the vaccine showed dysplasia of the cervix, whereas 53 from the placebo group did; and another 2 years later, two girls who received the vaccine showed dysplasia but when compared to the 112 girls with dysplasia from the placebo group, the effectiveness of the vaccine was undisputed.^[4] True to that, over the past decade, the HPV vaccines have shown high efficacy in preventing infections and lesions after immunization for up to 5–10 years, but they remain a recent development, and only time can tell the extent of their effectiveness in long-term use.^[5]

In 2015, an epidemiological study conducted in Europe to compare the benefits of the nonavalent and quadrivalent vaccine showed that there was a 19% more coverage of cancerous lesions with the nonavalent Gardasil and a 75% coverage regarding precancerous lesions.^[2]

Despite the merits, HPV vaccination in India has not gotten the start one expects it to have considering the prevalence of HPV; many factors can be attributed to this, including, but not limited to: A lack of education, a high cost, and a negative perception of side effects pertaining to past unsuccessful trials conducted in India. Although the WHO issued a safety update of the HPV vaccines in July 2017, based on the findings of the Global Advisory Committee on Vaccine Safety, the fear of side effects still prevails, and this fear can only be combated by the education of the masses, which brings us back to square one.

Need of the Hour: Education or Vaccination?

As stated above, without the public's proper education, bringing about the acceptability of the vaccine is no easy task; we have seen developed countries such as America struggle with implementing the vaccine due to hesitance stemming from a lack of adequate knowledge. To dwell deeper into the extent of public awareness in India, we can take a look into a study conducted in AIIMS, Jodhpur, where a total of 238 medical students, with representatives from each year, answered a questionnaire on cervical cancer. The results were undoubtedly thought-provoking, as only around 58%–60% of students had adequate knowledge on the risk factors and symptoms, while less than half (41%) knew the mortality associated with it. Similarly, while majority of them (80%) knew about the role of HPV in cervical cancer and anogenital warts, only around 60% knew about its association with penile and oropharyngeal cancers. If we break up the study group demographically: Considering gender, females had a statistically significant greater knowledge, and when

considering the year of study, the senior students had better knowledge compared to the juniors; highlighting the importance of medical education in promoting awareness.^[6]

A study undertaken on practicing physicians did not yield any hopeful results either; a questionnaire answered by 296 physicians from a district in Andhra Pradesh, majority of whom were: Male, working in either private practices or urban areas, and from the departments of general medicine, gynecology, or pediatrics; showed that while many knew about HPV in terms of its association with cancer, infectivity, pathogenicity, and vaccines available in the Indian market, less than half were aware of the screening and detection methods. Coming specifically to vaccination; more than half believed that the vaccine was costly, not effective, or not safe.^[7] When this is the state of HPV-related knowledge among medical students and medical practitioners, one does not need to wonder about the common man; whether it be in an urban or rural setting. This brings us to a question: Is the need of the hour education or vaccination? One can say that there are three preventive tools against invasive cervical cancer: Following preventive measures, screening, and HPV vaccination; what is the use of strengthening one when the other two are lacking? This question, or in simpler terms, the cost-effectiveness, with the cost here not only being monetary but also including the cost of time and efforts; forms the root of the debates regarding widescale implementation and inclusion of the vaccine into the immunization schedule.

Cost-Effectiveness of Human Papillomavirus Vaccine

The evidence from most of the available data analytics on HPV vaccination suggests that vaccination is indeed a very cost-effective method for the prevention of cervical cancer in India. Education alone though provides awareness, provides no means to prevent; one must include screening or vaccination; screening alone cannot be considered a solution either as there seems to be less acceptability to the common man. Vaccination is an easy solution providing both education and prevention; it can also help reduce the need of subsequent medical care, biopsies, and other invasive procedures associated with follow-up from abnormal cervical screening.

A comprehensive study showed that a combined effort of immunization for HPV among adolescent girls, alongside screening with VIA (Visual Inspection with Acetic acid) of females between 30 and 65 years of age appears to be the most cost-effective strategy at both 5- and 10-year frequencies.^[8] The inclusion of males however is still debated, especially in developing countries, as the result may be of less incremental value due to the herd immunity produced as a result of vaccinating females.^[9]

Country-specific implementation of quality intervention visits, school-based vaccinations, and centralized reminder and recall are some other cost-effective interventions aimed at increasing HPV vaccine coverage.^[10] Around the world, a steady increase in the HPV vaccination rates after a single time implementation of one of these intervention methods led the way toward a significant reduction in HPV cancers over the past half-decade; to refrain from including HPV in the immunization schedule should be a decision to be thought of twice; making sure to compare the benefits that one will achieve with the cost, time and energy that will be needed.

Conclusion

India, though contributing to nearly one-third of cervical cancer deaths worldwide, it is yet to implement HPV vaccination in large numbers; looking at the various reasons for this, we find that ultimately it stems down to a lack of education and subsequently acceptance. This along with inadequate implementation of screening procedures are a major reason for the inability to prevent HPV-associated cancers, cervical, or otherwise. Which route to take is a matter of government discretion, but from the discussion of effectiveness through analysis of previous methods employed and vaccination implementation in other countries; we can say that though implementation of screening is undisputed inefficiency, it has not shown high acceptability in Indians, whether educated or not; and the vaccine presents itself as a solution to the problems faced by screening, by being easy to understand, easy to accept and if backed by the government, and easy to avail. Therefore, inclusion of the HPV vaccine in the immunization schedule will undoubtedly give a platform to educate the public, and simultaneously provide a foolproof way to easily prevent disease that despite its preventable nature continues to be a major cause of loss in life.

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Conflicts of interest

There are no conflicts of interest.

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