HPV Vaccine, Let's Debate

by Dr. Maya Valecha, MD, DGO, Vadodara, Gujarat

Universal Health Organization

Date: 14 September 2022

Let us start with a question. Who has the authority to decide and declare the need, approval and inclusion of a vaccine in national program in India? For quite some time we see that it is the owner of the manufacturing company who does it first and then the government authority complies.

Serum Institute of India CEO Adar Poonawalla, on the sidelines of an event to celebrate the "scientific completion" of the vaccine, said: "The government of India will induct it in a few months in the national programme. It will be affordable." (1)

In spite of quite an uproar over how the Trials were conducted for HPV vaccine in 2009 when, "A standing committee later concluded that the study violated ethical norms and India's laws and regulations." And the fact that the Supreme Court is currently hearing a public interest litigation filed in 2012 raising questions about the trial and the vaccine.", India approved the two HPV vaccines in 2008 and they are available in the private medical sector and is being actively promoted through private schools. States of Delhi Punjab and Sikkim also included the HPV vaccine in their state immunization program. (2)

It is now necessary to have a widespread debate about the necessity, safety of this vaccine and some legal aspects also.

From the various scientific studies what has emerged is that Cervical Carcinoma is a disease where a virus can affect only when other factors, highly dependent on socioeconomic and health infrastructure of a country are present. Serious adverse effects are observed in other countries by HPV vaccine and there is no surety that the "vaccine" will prevent the disease. Likelihood of it being introduced in National Universal Immunisation Program has to be taken seriously with widespread debates and asking the government for explanation.

For the incidence of 0.0147% and mortality of 0.0092% at 55 to 59 years of age, we want to subject our little girls at the age of 9 to 15 to the risk of serious health issues of 0.0018%!

Whereas the infection is reported to occur between 26 to 35 years of age in India and the antibodies/protection is expected to last for 6 to 7 years, we want to give at 9 to 15 years of age.

Whereas the previous approval is subject to SC decision, the approval is being trumpeted as soon as the drug is produced.

The vaccine developed after initial 3 vaccines have to just show no persistent infection for 6 months after the vaccine. And, as per WHO guidelines no long-term studies are required now! That is serious. Because in 95% of the cases infection resolves even by itself what we want to know is effectivity in preventing the disease and adverse effects of the new vaccine

The lessons learnt by Japan with ultimate withdrawal from active recommendation are very important.

"The human papillomavirus (HPV) vaccine has been linked to a number of serious adverse reactions. The range of symptoms is diverse and they develop in a multi-layered manner over an extended period of time. The argument for the safety and effectiveness of the HPV vaccine overlooks the following flaws: (i) no consideration is given to the genetic basis of autoimmune diseases, and

arguments that do not take this into account cannot assure the safety of the vaccine; (ii) the immune evasion mechanisms of HPV, which require the HPV vaccine to maintain an extraordinarily high antibody level for a long period of time for it to be effective, are disregarded; and (iii) the limitations of effectiveness of the vaccine. We also discuss various issues that came up in the course of developing, promoting and distributing the vaccine, as well as the pitfalls encountered in monitoring adverse events and epidemiological verification." (14)

> "Japan's efforts to stop active recommendation might have been successful because of its historical background of cases of environmental pollution and drug-induced suffering (Minamata disease, thalidomide, SMON, dura mater graft-associated Creutzfeldt–Jakob disease, HIV transmitted by contaminated blood products, etc), which occurred during the post-war period of rapid economic growth. In the multi-plaintiff suits that followed the instances of environmental pollution and drug-induced suffering, the plaintiff groups sought not only compensation for damages, but also institutional reform and revisions to the law to prevent the repetition of the same mistakes (62).

This historical background has created a situation in which the mass media and regulators cannot easily ignore the victims' complaints about the side-effects of new vaccines." (14)

Without even proper screening facilities, with the general awareness in cleanliness and other risk factors the incidence and mortality are declining in India. Introduction of this vaccine is waste of public resources. What is recommended is the same funds should be used for improving nutritional and hygienic conditions for adolescent girls, screening for women with known risk factors and those coming for any gynaecological check-up and if suspicious lesion found.

We have to be doubly vigilant on this because WHO, without giving specific data of efficacy or adverse effects, has celebrated the inclusion of HPV vaccine in 100 countries in their National Immunization program.

"Next year, the World Health Assembly will discuss a Draft Global Strategy for the elimination of cervical cancer as a public health issue, presented for approval, which will provide countries with targets and strategic actions for countries in their efforts." (13)

As we have experienced during Covid-19, WHO guidance is implemented in our country without gathering all the facts of our country involving maximum number of opinions in the decision making.

Below mentioned facts as they have emerged through various studies strongly suggest that inclusion of HPV vaccine is not required and even in private sector it should not be actively promoted without informing the adverse effects:

- HPV has been found to be a necessary but not sufficient cause for cervical cancer. (3)
- Specific types of oncogenic HPV-16, 18 have been identified in patients with cervical cancer. Other epidemiological risk factors are early age at marriage, multiple sexual partners,

multiple pregnancies, poor genital hygiene, malnutrition, use of oral contraceptives, and lack of awareness. (3)

- In Maharashtra, high-risk HPV was associated with increasing age, low education level, manual work, early age at first sexual intercourse, and widowhood/separation. (3)
- The current cervical carcinogenesis model includes three steps of HPV infection, progression to high-grade preinvasive lesions, and invasion. ***More than 95% of infections, including those with cytological abnormalities, resolve spontaneously, returning to HPV DNA negativity with seropositivity.*** (2)
- Being vaccinated does not guarantee protection against cervical cancer because the HPV strains that the available vaccines protect against are not the only strains that can cause cancer. (2)
- The biggest task will be in allocating adequate resources and manpower for vaccinating the massive demographic of adolescent girls aged between 9 and 15, to ensure that they are protected from HPV early on. (4)
- Dr Rajesh Gokhale, Secretary, Department of Biotechnology, told The Indian Express that antibodies developed after the two doses can last between six and seven years and, unlike Covid-19 vaccines, boosters may not be required for the cervical cancer vaccine. (5)
- In Indian women HPV infection is common at 26–35 years of age, which is a decade later than that in developed countries, and cancer occurs between 45 and 59 years of age. (3)
- HPV vaccines have performed over the past decade show that the two vaccines have high efficacy, preventing infection and lesions for between five and 10 years after immunisation. However, the HPV vaccines are only a recent development and there is no long-term data available to indicate for how many years the vaccine will remain effective. (This in 2014, 7 years is not enough for this kind of vaccine.) (6)
- "The data will only start coming in when we are able to follow up with girls who have been vaccinated for 20, 30 or 40 years," said Anant Bhan, researcher on bioethics, global health and policy. "So, we need good post-marketing surveillance." (2)
- Any vaccine has potential side effects. What many public health specialists are advocating is simply that before the vaccine is introduced, the immunisation programme establish efficient systems to pick up and report adverse events, provide treatment and compensation to those affected, and be ready to suspend the vaccine, if necessary. The government should also be transparent and share data on the basis of which it decides whether or not to use the vaccine. (2)
- said Sarojini of SAMA. "Evidence so far from other countries' experiences shows that cervical cancer rates and mortality rates have come down because of screening programmes." (2)
- This series of vaccinations is highly likely to protect her from HPV infection until she enters

> the routine screening program, whether that be primary HPV testing or a combination of HPV testing and cytology. **Future studies of prophylactic HPV vaccines, as defined by the WHO, must demonstrate protection against six month type specific persistent infections, not actual cervical cancer precursor disease endpoints, such as cervical intraepithelial neoplasia grade 3 (CIN 3) or adenocarcinoma in situ (AIS).** This simplifies and makes less expensive future comparative studies between existing and new generic vaccines. (7) (Emphasis added)

Why did they discontinue the Gardasil vaccine?

- They cited **a lack of adequate long-term testing of the vaccine, unproven efficacy and disturbing news of adverse side effects such as neurological disorders**. (8)
- In January 2018, the National Technical Advisory Group on Immunisation, the highest technical body on vaccination, gave its approval to the introduction of the cervical cancer vaccine in India's universal immunisation programme, **subject to the outcome of a 2012 case in the Supreme Court regarding adequate clinical trials of the vaccine — which still remains pending.** (9)
- Reports of serious health issues after HPV vaccination were consistently rare—around 1.8 per 100,000 HPV vaccine doses, or 0.0018%. A total of 758 serious health problems that arose after HPV vaccination were reported in VAERS during that time. Meanwhile, the rate of nonserious health issues following HPV vaccination reported in VAERS dropped from 43 to 28 per 100,000 vaccine doses. (10)
- At 4 years follow-up, the HPV vaccines decreased HPV-related precursors to cervical cancer and treatment procedures but increased serious nervous system disorders (exploratory analysis) and general harms. As the included trials were primarily designed to assess benefits and not adequately designed to assess harms, the extent to which the benefits outweigh the harms is unclear. (11)
- Limited access to clinical study reports and trial data with case report forms prevented a thorough assessment. An independent assessment of the complete individual participant data is needed. (11)
- This study concludes that the overall incidence and mortality of cervical cancer showed a significant decreasing trend in India between 1990 and 2019, the highest decline in the incidence and mortality rates were reported in the period 1998-2005. (12)
- "In India, the age-standardized incidence rate is 14.7 per 100,000 women, and the age-standardized mortality rate is 9.2 per 100,000 women [3]." (0.0147% and 0.0092%) (12)

- Mortality due to cervical cancer among women in India in the period 1990-2019 "that cervical cancer mortality has decreased over time while the decrement in mortality is not uniform over time. Jammu & Kashmir have the lowest mortality level (4.59 per 100,000 women in 1990, 3.93 per 100,000 women in 2000, 3.57 per 100,000 women in 2010 and 3.38 per 100,000 women in 2019) whereas Tamilnadu records the highest mortality due to cervical cancer(20.73 per 100,000 women in 1990, 18.62per 100,000 women in 2000, 13.53 per 100,000 women in 2010 and 11.56per 100,000 women in 2019) from 1990 to 2019. Maps in Fig. Fig.22 show that decrement in the incidence is not uniform across the states over time. Some of the states like Jharkhand (-30.42%) and Gujarat (-27.00%) show the highest percentage decline in mortality due to cervical cancer in the period 1990-2000. Further in the next decennial (2000-2010), West Bengal (-33.83%) followed by Himachal Pradesh (-33.02%) have the highest percentage decrement in cervical cancer mortality. Overall, from 1990 to 2019, Jharkhand (-56.16%) recorded the highest percentage decrement, followed by the Himachal Pradesh (-53.37%)"
- Conclusion

  Though the incidence and mortality of cervical cancer declined over past three decades but it is still a major public health problem in India. Information, education and communication activities for girls, boys, parents and community for the prevention and control of cervical cancer should be provided throughout the country. (13)

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