Human Papilloma Virus Vaccination and its Future in Pakistan; Are we ready yet?

Approximately 5% of all cancers worldwide are caused by HPV. In United States, 3% of all cancers in women and 2% among men are caused by HPV.[1] A variety of malignancies and pre-malignancies are linked with HPV. HPV is associated with almost all of cervical cancers with HPV type 16 and 18 associated with 70% of all cases.[2] HPV causes about 95% of anal cancers with HPV 16 accounting for most of them. About 70% of oropharyngeal cancers are caused by HPV.[3] HPV is associated with various other cancers as well. In United States, it causes 65% of vaginal cancers, 50% of vulvar cancers and 35% of penile cancers with majority of them caused by HPV type 16.[4]

The trend of Human Papilloma Virus led cancers are showing a rising trend in Pakistan. According to Cervical Cancer Global Crisis Card (CCGCC), Pakistan ranks seventh in terms of annual death count due to cervical cancer. Cervical cancer ranks as third leading cause of female cancer mortality in Pakistan.[5]

HPV 6 and 11 are low risk viruses causing genital warts whereas HPV 16 and 18 are considered high risk accounting for 70% of cervical cancers. In developing countries, cancer treatment costs keep increasing with poor survival rates with patient burden borne by society at large. It is essential to identify a target age and population for screening and vaccination to have a significant impact; data suggests that by Quality adjusted life years (QALY) measurement, cost effective vaccination with maximum impact should happen in adolescent age.[6]

Two vaccines, quadrivalent HPV vaccine Gardasil-4 and bivalent HPV vaccine Cervarix were developed. The former covers HPV types 6, 11, 16 and 18 while the latter covers HPV types 16 and 18. These vaccines are highly effective when administered before sexual activity. WHO recommends two doses of these vaccines spaced 6-12 months apart, for girls aged 9-13. Gavi-the Vaccine Alliance provides subsidies to introduce vaccinations in Low and Middle income countries.[7]

According to a study in Lancet, to analyze cost effectiveness and health effects of vaccination program, a Microsoft Excel Based model called Pappiloma Rapid Interface for Modelling and Economics (PRIME) was established. The system accounted for vaccination effectiveness before sexual debut and correlated with cervical cancer burden and mortality.179 country data with a vaccination cohort of 58 million adolescent females were studied. Using the PRIME model, it was determined vaccination prevented 690 000 new cases of cervical cancer and 420 000 deaths mostly in low and middle income countries at a cost of USD 4 billion. In 87% of the studied countries, every disability adjusted life year (DALY) averted costed less than the Gross Domestic Product (GDP) of the country, making the vaccination very cost effective.[8] Pakistan is a GAVI supported country, however the absence of HPV vaccination program has kept the market price for vaccination high and out of reach for the majority population.

Safety and efficacy of HPV vaccinations have been demonstrated by many studies in the past.[9] However, HPV vaccine has had concerns in Japan which led to its drop of vaccination coverage from 70 percent to just 1 percent.[10] In spring of 2013, the media repeatedly reported pain and motor disability in girls receiving vaccination even though it is not evidently clear if these effects are caused by the vaccine. The Japanese Ministry of Health, Labour, and Welfare suspended its active recommendation for girls to receive HPV vaccinations in June, 2013 decreasing coverage significantly. According to a study in Lancet Oncology, Japanese women who became adolescent between 1993-2008 are at increased risk of developing cervical cancer. The calculated risk significantly increases each year with girls who became adolescents when vaccine was discontinued at a higher risk compared to girls who were adolescent when the vaccine was introduced.[11]

As much as there is need for HPV vaccination, the question arises if we are ready as a society for a successful vaccination program. This dilemma could be understood from different perspectives. There is a difference between low and middle income countries and high income countries in terms of annual cervical cancer incidence and it would be unfair to label such a huge difference in numbers only due to preventive strategies. There is marked differences in educational levels, knowledge of cervical cancer, access and awareness. Also, there is deep rooted stigma associated with the disease which pose barriers to access.

Another way of understanding this problem is to look at another vaccination program involving similar age group and population. A study was conducted to access tetanus toxoid (TT) vaccine in women of childbearing age in Karachi due to high incidence of neonatal tetanus despite vaccination program introduction. Over 50% of women did not receive vaccination and non-vaccination predictors included young age without formal education, poor knowledge about disease process and complications, living with extended family, poor family support and other members of family making decisions related to women's health.[12]

It is very important to prevent HPV associated cancers especially in low and middle income countries where there is huge economic and social burden due to cancer morbidity and mortality on society. GAVI drew very important conclusions from their HPV demonstration projects and suggests School Based delivery works, grassroots communication, integration with routine immunization and delivery with other health programs. However, it is equally essential to understand local

parameters. One such example is school based delivery networks might not work in Pakistan since there is only 44% female enrollment in schools.[13] Therefore, social and cultural dynamics and tailored supportive strategies are needed to engage communities to improve their knowledge, attitudes and practices. By doing that, we can achieve successful coverage of introduced vaccination HPV program.

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