

Shift of Cervical Vaccine Regime: 3-2-1

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Cervical cancer is by far one of the major cause of cancer mortality in female population. In India, burden of cervical cancer mortality is ranging from 6-29% of total cancers occurring in females. Highest age adjusted incidence rate is seen in Mizoram which is 23.07/1 lakh female population and lowest is seen in Dibrugarh which is 4.91/ 1 lakh female population. As per Ahmedabad Population based cancer registry report 2016, incidence of cervical cancer is 9.04/1 lakh population in Ahmedabad. As per World Health Organization (WHO),¹ around 6,00,000 females got diagnosed with cervical cancer every year and 3,00,000 women add to cervical cancer mortality. In other way this means across the globe one woman dies of cervical cancer every 2 minutes. WHO also states that around 90% of cervical mortality comes from low to middle income countries.

To mitigate huge burden of cervical cancer morbidity and mortality, WHO in association with World Health Assembly has given Global Strategy for cervical cancer elimination in 2020.¹ Main indicators of these strategy are to vaccinate 90% of females with Human Papillomavirus (HPV) vaccine by 15 years of age, 70% of cervical cancer cases should be screened by high performance cervical screening test and to treat 90% of pre cervical cancer cases. All countries need to achieve above parameters by 2030, which will help us to eliminate cervical cancer by next century.

Cervical cancer vaccine was first found in 1990 by an Australian Scientist and in 2008 Cervarix was the first cervical vaccine (Bivalent) to be marketed followed by Gardasil (Quadrivalent) in 2012. Initially in 2008, this vaccine was given in 3 dose regime 0,1-2,6 months to adolescent girls with age of 12-13 years with catch up period of 13-18 years, then by 2014 two dose regime was introduced as 0,6 months. However, then after there was no standardized regime for cervical vaccine, some countries continue 3 dose regime and some were giving 2 dose regime. However, in many HPV vaccine trails and from real world national immunization programme there were vaccine defaulters and their data showed protection against cervical infection, which laid foundation of single dose HPV vaccine studies. Suspension of HPV vaccine trail by

International Agency for Research Cancer (IARC) contributed immensely in providing single dose vaccine data. The Gujarat Cancer and Research Institute (GCRI) was also part of this study.

These research initiated plethora of questions like : is it biologically plausible? Will it protect against persistent HPV infection? Will it protect against CIN2+ lesions? How long will immunity last? By 2018, many researches started coming up with single HPV vaccine dose showing protective effect against preventing cervical infection by HPV. As per data shown by Costa Rica² HPV vaccine trail, single HPV vaccine dose provides stable antibodies level against HPV 16 stain even at 11 years. Kreimer et al and Harper DM et al also showed that single dose HPV vaccination provides consistent mean antibodies level against HPV 16 and HPV 18 even after 10 years and is almost parallel to two and three dose regime.^{3,4} Sankaranarayanan, et al showed that incidence of HPV infection was same among one dose, two dose and three dose groups. He also showed that there was no case of persistent infection among any of the groups.⁵ Verdoodt et al also shows data from Danish national immunization programme which states 62% reduction in CIN3 cases irrespective of number of vaccine doses.⁵

In 2019, Strategic Advisory Group of Experts on Immunization (SAGE) has advised countries can consider a “1+1” schedule with an extended interval for the administration of the second dose with gap up to 3-5 years in younger girls aged less than 15 years. It was advised to give one dose to adolescent girls followed by a delayed second 3-5 years later, while we get more robust data from continue trials. By that time we may be able to decide whether second dose is needed or not. Vaccination of boys may be kept on hold to allow better coverage of girls. In 2021, Joint Committee on Vaccination and Immunisation (JCVI) of United Kingdom has agreed that there is now enough evidence to advise a change in the schedule from 2 doses of HPV vaccine to one dose. To boost this, finally in 2022 WHO has stated that “One-dose HPV vaccine offers solid protection against cervical cancer”.⁶

To conclude I would say, all low to middle income countries should actively participate in Cervical Cancer Elimination strategy 90-70-90 and as per recent advice by WHO, they should start offering single dose HPV vaccine to young females with age group of 9-20 years and two dose regime (6 months apart) to females more than 20 years. Single dose administration will be highly cost effective and will provide at par protection in comparison to two and three dose regime. For India, I would recommend to start cervical vaccination programme at every government medical college, cancer hospital and finally to roll out cervical vaccination in national immunization schedule with one dose strategy.

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