

Editorial

Human papillomavirus & cervical cancer: Looking ahead

About three and a half decade ago the link between Human Papillomavirus (HPV) and cervical cancer was proposed by Harald zurHausen. Today HPV infection is known to cause about 5 per cent of global burden of human cancers and in females it accounts for over 60 per cent of all infection-related cancers. It is now well established that HPVs are important human carcinogens causing not only cervical cancer but also substantial proportion of anogenital, head and neck and skin cancers. In addition, HPV can be detected in carcinomas of several other organ sites in humans but the carcinogenic role of HPV in these cancers is yet to be established.

Cervical cancer is the most common cancer and leading cause of cancer deaths in women in developing countries. India shares about 25 per cent of global cervical cancer burden and almost all cases harbour high risk HPV infection. This is a unique cancer in the sense that it is totally attributable to the effects of an infectious virus, HPV which is epitheliotropic in nature. Numerous clinico-epidemiological, molecular and experimental studies have confirmed a strong correlation between HPV infection and development of premalignant and malignant lesions of the uterine cervix in women. It is also established that the disease is caused by persistent infection of one or more of 15 known high risk types of Human papillomaviruses out of more than 100 HPV genotypes described so far.

Recently, two HPV prophylactic vaccines, Cervarix and Gardasil based on papillomavirus like particles (HPV-VLPs) are produced by self-assembly of the major viral L-1 capsid protein using recombinant DNA technology. Both have been shown in several large clinical trials to be safe, well tolerated and can induce strong immunity against the HPV genotypes incorporated in the vaccine. This is the first antiviral vaccine developed specially to prevent human cancer.

Since these viruses are also associated with the development of several other cancers, benign warts and papillomas, it should equally be effective in preventing these diseases.

Although at least 15 high risk oncogenic HPVs are known, vaccines against only two of them – HPV type 16 and HPV 18 may create selective immunologic pressure to raise prevalence of cervical cancer due to emergence of nonvaccine related HPV genotypes. However, such assumption can only be tested in the time to come.

Since development of cervical cancer takes 10-15 yr, demonstration of a vaccine intervention that prevents cancer, would require a long term observation of a large number of vaccinated women. In addition, there are several issues particularly social, economic and ethical issues associated with vaccine implementation in developing countries such as India where cervical cancer is still a most common cancer in women. Also, the number of doses, the cost and durability of immune protection and whether men should be vaccinated or not- are other important concerns associated with HPV vaccination program particularly in low resource settings. Recently, Drug Controller General of India (DCGI) has approved introduction of one of the HPV vaccines, 'Gardasil' in India. But no national guidelines have been developed. Nor any initiative has been taken to consider if HPV vaccine could be incorporated in the universal infant immunization program alongwith other vaccines.

Efforts are also being made to develop therapeutics as well as cost-effective second generation HPV vaccines including anti-HPV therapeutics such as carragenan curcumin and neem which need further study for establishing clinical efficacy of these compounds.

Realizing an immediate importance of HPV vaccine in India and to understand the pros and cons of

the vaccine implementation programme and to generate knowledge and awareness, this special issue of IJMR with articles from reputed scientists and clinicians of India and abroad working in the field of cervical cancer and HPV vaccine has been brought out. The topics covered include the magnitude of the disease and HPV prevalence¹⁻³, role of screening, newer and cost-effective screening tools such as VIA, Care HPV and their clinical utility in relation to PCR and HC 2⁴⁻⁶, current and future second generation vaccine efforts^{4,7-12} including anti-HPV therapeutics and immunology of HPV infection¹³⁻¹⁶.

Though global burden of cervical cancer may eventually be reduced through universal immunization, at present HPV vaccine will supplement rather than replace cervical screening program.

Bhudev C. Das*, Alok C. Bharti & Mausumi Bharadwaj

Institute of Cytology & Preventive Oncology (ICMR)
1-7, Sector 39, NOIDA 201 301, India

*Present address & correspondence:

Dr B.R. Ambedkar Center for Biomedical Research
University of Delhi, Delhi 110 007, India
bcdas48@hotmail.com

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