

Human papillomavirus: The silent intruder

Sir,

We read with both interest and disappointment, the review article 'Emerging trends in prevalence of viral STI's recently published in your prestigious journal.^[1] Interest is due to the fact that the article comprehensively addressed prevalence and trends of HIV and other viral STI's across the length and breadth of India but disappointment aroused because the 'silent epidemic' of HPV infections was not

sufficiently discussed. High risk HPV infections have gained prominence in the last two decades and have been implicated in the development, maintenance and progression of cervical cancer. Harald zur Hausen was awarded the Nobel prize for his discovery of “human papilloma viruses causing cervical cancer” in October 2008. His work led to better understanding of mechanisms of HPV-induced carcinogenesis and development of prophylactic vaccines against HPV acquisition. HPV infections are common in young women after the onset of sexual activity but most newly acquired HPV infections are cleared spontaneously and the prevalence drops from a peak in adolescents and young women. Worldwide human papillomavirus (HPV) prevalence in women with normal cytology at any given point in time is approximately 10% indicating that HPV is one of the most common sexually transmitted infections. HPV-16 is consistently the most common type and HPV-18 the second with some minor regional differences. A study from North India pegged high-risk HPV positivity in normal women at 10% with HPV 16 being the commonest, while in rural South Indian women an overall prevalence of 16.9% was reported across all age groups (16-59 years).^[2,3] The HPV testing methods used in both the studies was polymerase chain reaction (PCR) for HPV testing. HPV testing has been found to be highly sensitive but low in specificity and therefore has to be used in conjunction with cytology/colposcopy. The negative predictive value of the test is about 99%.^[4]

In a recent cluster-randomized trial involving 52 village clusters of Osmanabad district, Maharashtra, high-risk HPV positivity in women between 30 and 59 years was 10.3%. In this landmark trial, patients who were positive by cytology, HPV testing or visual screening tests underwent colposcopy and directed biopsy and those with cervical precancer or cancer were treated. After eight years of follow-up, it was found that deaths due to cancer in the HPV tested group were significantly lower compared to the unscreened or other screening groups. The reduction in the incidence of cancer deaths associated with HPV testing probably reflects the higher sensitivity of HPV testing to detect lesions with a high potential for malignant transformation than that of cytology or visual screening tests.^[5]

The burden of cervical cancer in India is high with more than 100,000 new cases reported annually out of roughly 500,000 cases worldwide. Screening with Pap test has failed to bring down this dreaded

cancer over the last five decades in India. Organized screening programs using Pap test in India were difficult to implement because of logistic problems and the window of opportunity to decrease cervical cancers was lost. The strong causal relationship of high risk HPV and cervical cancer has resulted in the development of a number of HPV DNA testing systems. HPV detection assays are automated, objective and sensitive unlike cytology which is labor intensive and less sensitive in the diagnosis of cervical intraepithelial neoplasia. The hybrid capture 2 (HC2, Qiagen Inc., formerly Digene) is approved by FDA for screening in women over 30 along with cytology. This test detects 13 most common high risk HPV types. From a meta-analysis in both developed and developing countries, it was seen that HPV DNA testing was more sensitive than cytology in detecting high grade CIN and has been recommended for primary screening in women over 30 years in Europe.^[4] However, the cost per test is still high as \$20-\$30. A new rapid HPV test – *CareHPV* detects 14 high risk HPV types, is more affordable, simpler and faster, the report being available in less than 3 h. However, this test is still being validated and may become available in the near future and may be used in STD and preventive oncology clinics, the target group being sexually active women over 30 years.^[5]

Sex education and awareness about HPV infections is necessary among vulnerable young girls and boys who are yet to initiate sexual activity. Primary prevention of HPV infections and cervical cancer with vaccination is most effective in sexually naïve girls. The currently available vaccines can protect about 70-80% of cancers caused by HPV-16 and 18, but long-term efficacy is yet to be seen. Thus, screening will have to continue, as before, till new guidelines are formulated in the post vaccine era. For a deeper impact of vaccination on reduction of cervical cancers, the co-operation of various governmental and non-governmental organizations are required to deliver it to those who need it the most and not just to those who can afford the vaccine.

Shalini Rajaram, Sumita Mehta, Neerja Goel

Department of Obstetrics & Gynecology, University College of Medical Sciences & Guru Teg Bahadur Hospital, Delhi – 110 095, India

Address for correspondence: Dr. Shalini Rajaram,
Department of Obstetrics & Gynecology, University College of
Medical Sciences & Guru Teg Bahadur Hospital,
Delhi - 110 095, India.

E-mail: rajaram.shalini@gmail.com

DOI: 10.4103/0378-6323.72446 -

REFERENCES

1. Dhawan J, Khandpur S. Emerging trends in viral sexually transmitted infections in India. *Indian J Dermatol Venereol Leprol* 2009;75:561-5.
2. Singh A, Datta P, Jain SK, Bhatla N, Dutta Gupta S, Dey B, *et al.* Human papilloma virus genotyping, variants and viral load in tumors, squamous intraepithelial lesions, and controls in a north Indian population subset. *Int J Gynecol Cancer* 2009;19:1642-8.
3. Franceschi S, Rajkumar R, Snijders PJ, Arslan A, Mahé C, Plummer M, *et al.* Papillomavirus infection in rural women in southern India. *Br J Cancer* 2005;92:601-6.
4. Cuzick J, Arbyn M, Sankaranarayanan R, Tsu V, Ronco G, Mayrand MH, *et al.* Overview of human papilloma virus based and other novel options for cervical cancer screening in developed and developing countries. *Vaccine* 2008;265:K29-41.
5. Sankaranarayanan R, Nene BM, Shastri SS, Jayant K, Muwonge R, Budukh AM, *et al.* HPV screening for cervical cancer in rural India. *N Engl J Med* 2009;360:1385-94.