



HPV Test As Primary Screening Tool

Priya Ganesh Kumar*

Department of Preventive Oncology, Medical Director of Sainiwas Healthcare, India

***Corresponding Author:** Priya Ganesh Kumar, Department of Preventive Oncology, Medical Director of Sainiwas Healthcare, India.

DOI: 10.31080/ASWH.2022.04.0371

Received: April 22, 2022

Published: May 06, 2022

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Abstract

WHO Mission statement of Cervical cancer Elimination by 2030 has been a historic moment and has created an impactful global awareness regarding this deadly disease. The triple formula of 90-70-90 has been designed to have a 30% reduction in mortality from cervical cancer to be achieved by 2030. The goal of Cervical cancer elimination is to bring down the cases of cervical cancer below 4 per 100,000 woman. To achieve this goal the targets laid down is 90% coverage of girls fully vaccinated with HPV Vaccine by 15 years of age, 70% of women screened with an HPV test at 35 and 45 years of age and all managed properly, 90% of women identified with preinvasive disease receive adequate treatment and follow up. It is now an established fact that cervical cancer is caused by persistent infection with high-risk HPV strains. 4 out of 5 women in our country is affected with HPV, HPV being a sexually transmitted virus. Persistent high risk (HR) HPV is necessary for development of precursor lesions and cervical cancer. The major steps in cervical carcinogenesis include HPV infection, HPV persistence for a certain period of time, progression to precancer and invasion

Keywords: HPV; Cervical Cancer; Screening

Introduction

WHO Mission statement of Cervical cancer Elimination by 2030 has been a historic moment and has created an impactful global awareness regarding this deadly disease. The triple formula of 90-70-90 has been designed to have a 30% reduction in mortality from cervical cancer to be achieved by 2030. The goal of Cervical cancer elimination is to bring down the cases of cervical cancer below 4 per 100,000 woman. To achieve this goal the targets laid down is 90% coverage of girls fully vaccinated with HPV Vaccine by 15 years of age, 70% of women screened with an HPV test at 35 and 45 years of age and all managed properly, 90% of women identified with preinvasive disease receive adequate treatment and follow up. As per cancer registry GOI, there has been a slow decrease in the ASR of Cervical cancer. As per 2019 figure ASR/100000 Cervical cancer is 13.5 (India) with high figures in certain states of India - Karnataka - 20.9, Chattisgarh 17.6, Madhya Pradesh 15.9 [1]. Low incidences are found in Kerala 9.9, Goa 7.9, J&K 7.6. This slow reduction in the incidences of cervical cancer

has been due to the efforts put by various health care providers in public and private sector, albeit the fact that India lacks systematic registry, reporting system and case management for precancerous conditions. As per the latest GLOBOCAN 2018 India leads the globe next to China with Age standardized Incidence rate for India 14.7, world 14.7, Australia 6.0, UK 6.8. Age standardized. Mortality rate for India 9.2, world 6.9, Australia 1.7, UK 2.1. As per the GLOBOCAN 2018 in India new cases annually reported are 96,922 with 60,078 deaths annually due to cervical cancer; one lady loses her life every 8 minutes with 200 women dying daily due to cervical cancer.

As per Globocan 2020, the incidence of new cases of cervical cancer in India is 1,23,907 accounting for 18.3% of all the cancer cases in India. It is second leading cause of deaths due to cancer after Breast Cancer with 77,348 deaths per year.

HPV as the major causative factor for cervical cancer

It is now an established fact that cervical cancer is caused by persistent infection with high risk HPV strains. 4 out of 5 women in

our country is affected with HPV, HPV being a sexually transmitted virus. The prevalence of HR-HPV in women with normal cervical cytology varies among the different regions of the world. Global HPV prevalence was estimated to be approximately 12%, higher prevalence were noted in sub-Saharan Africa 24% [2,3].

Crude age-specific HPV prevalence (%) and 95% confidence interval in women with normal cervical cytology in India

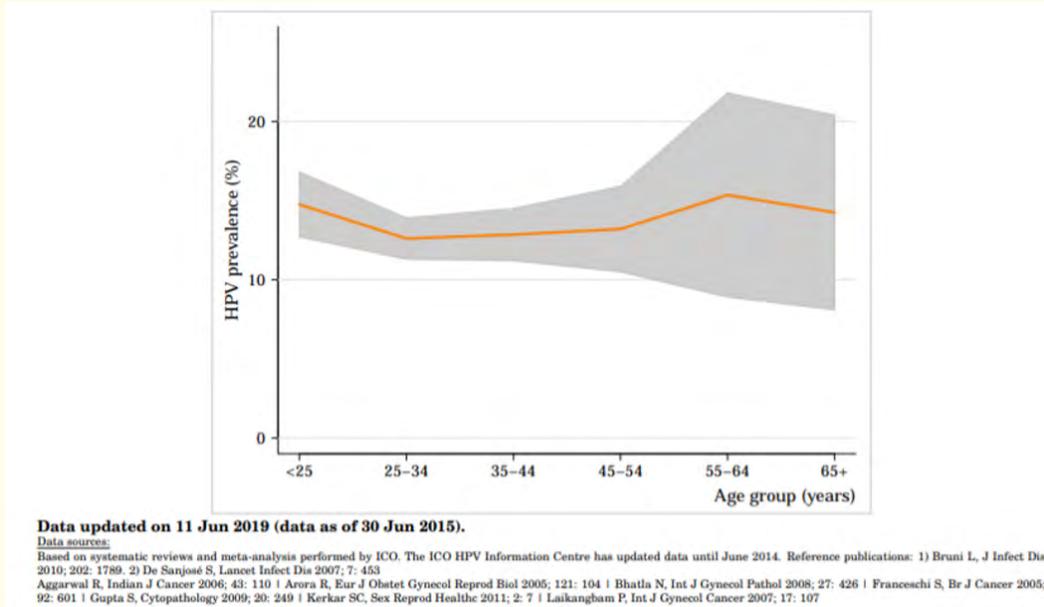


Figure 1

Usually HPV infection being a local infection is symptomless and doesn't evoke any systemic inflammatory reactions. Most of the HPV positive cases turns negative with in 8-12 months. Persistent high risk (HR) HPV is necessary for development of precursor lesions and cervical cancer. The major steps in cervical carcinogenesis include HPV infection, HPV persistence for a certain period of time, progression to precancer and invasion [4].

Recommendations for screening

- ACS recommends" the primary HPV test" as preferred test for cervical cancer screening for ladies 25-65 rears of age (A Primary HPV test is an HPV test that is done by itself for screening).
- FOGSI GCPR recommends HPV test as Primary Screening test in good resource setting and VIA in limited resource setting for

ladies from 30-65 years. A single visit approach is encouraged and treatment may be offered based on Colposcopy diagnosis ('see and treat) or even on the basis of HPV test or VIA results ('screen and treat) [5].

- In an Indian study, even a single round of HPV testing was shown to significantly reduce the incidence of cervical cancer [6].

Validated HPV tests

- Cobas 4800 by Roche Diagnostics - RT-PCR Genotyping test which identifies 14 high risk strains -HPV 16, HPV 18 and other 12 high risk strains. This test is approved for Primary cancer screening
- Hybrid Capture 2 which estimates 13 high risk HPV by hybridization technique.

- **Frequency-** Every 5 years from 30-65 years.
- **Collection-** This test is collected in the LBC container similar to LBC collection.

Screening paradigms and FOGSI good clinical practice recommendations

HPV as primary screening method

In good resource settings HPV positive cases should be triaged with either genotyping or cytology. If HPV 16/18 positive or cytology result is abnormal (ASCUS or higher), then referral to colposcopy. In case of Non HPV 16/18, repeat the HPV test after 1 year. The risk of CIN 3+ in HPV 16/18 positive cases is 21.1% while it is 5.4% [7] with other non 16/18 strains. Hence HPV 16/18 positive cases should be directly referred for colposcopy guided biopsy and non 16/18 to be triaged with cytology or VIA.

In limited resource settings, VIA can be used to triage HPV positive women.

Co-testing as screening method (HPV+Cytology)

- Women with both HPV positive and cytology abnormal should be advised colposcopy and directed biopsy.
- Women with HPV positive and cytology negative should be advised HPV genotyping or repeat co test after 1 year.
- Women with HPV negative and cytology abnormal should be advised further follow up depending on the type of cytological abnormality. All cases with ASC-H, atypical glandular cells or suspected cancer are referred to colposcopy irrespective of HPV test results.

Limitations observed in adopting HPV as primary screening method by HCP in India

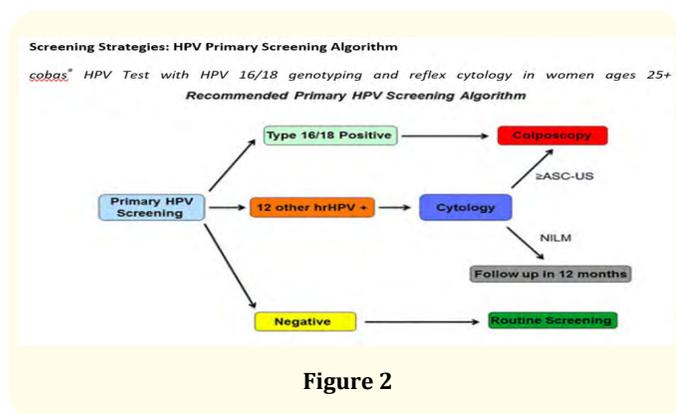
- The concept of screening is yet not rooted.
- Cost factor
- Unavailability
- Inefficiency in managing HPV positive cases due to unavailability of trained manpower or limited resources.
- Social stigma-HPV related to sexually transmitted infection is related to social taboo
- In Google tech savvy era, unpreparedness of HCP to handle the apprehensions of HPV positive patients as HPV related to cervical cancer.
- Fear factor in women to come to the health facility.

Methods to cope up these limitations

- HCP in India both in public and pvt sectors need to emphasis on regular screening for themselves and for any women irrespective of any symptoms.
- HPV test to be made mandatory by Insurance companies while issuing new policy and 5 yearly HPV test to be made compulsory factor for renewing the policy
- To make Validated HPV test available at various accredited Laboratories and Govt set ups
- To upgrade the existing health care facility with necessary equipment and technology
- Effective methodology to spread the awareness and knowledge of HPV through various Social media, thus removing the stigma associated with HPV
- Empathetic counselling while advising HPV test
- Providing Self HPV collecting kits to avoid coming to the facility.

Conclusion

Screening of the ladies for cervical and breast cancer should be taken as a prime responsibility by all the clinicians. WHO has declared Cervical elimination by 2030 i.e. less than 4 cases of cervical cancer per100000 women. The irony is that cervical cancer is the only cancer which can be preventable, yet not prevented. Systematic approach at all the three levels - Primary level with



vaccination, Secondary level with regular screening, Tertiary level with case management should be followed judiciously to achieve the GOAL of WHO 90-70-90 Mission.

“Lets us all join hands to make India cervical cancer free”.

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