



CANCER FOUNDATION OF INDIA

# Primary and Secondary Prevention of Cervical Cancer in India

## Summary Report

Roundtables

Gangtok | Delhi | Chennai  
2014

## BACKGROUND AND OBJECTIVES

In compliance with the UN declaration on the prevention of Non-communicable diseases (September 2011), the Government of India launched National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) by merging National Programme for Cancer control (NPCC) with other non-communicable diseases. Furthermore, a GOI-WHO Biennial National Action Plan and Monitoring framework was also established in 2012-13 to prevent NCDs. Thus, India is fully committed to strengthen its health system to meet the objectives of global action plan as per suggested time-frame, which targets a 25% relative reduction in mortality from NCDs including cancer by 2025.

This indeed calls for a robust policy planning and implementation towards prevention and early detection of high risk cancers such as tobacco associated and HPV infection related cancers. While a comprehensive anti-tobacco policy and a proper legislation is already in place to curb tobacco usage, the country is yet to have a feasible national policy on primary and/or secondary prevention of cervical cancer.

The cancer of Cervix Uteri (Cervical cancer) is the most common cancer amongst women in India, accounting for over 123,000 new cases and more than 73,000 deaths annually. It is now well established that cervical cancer and its precursor lesions are caused by persistent infection by one or more high-risk HPV types. As per recent data the infection with HPV 16 and 18 accounts for over 80.0 % cervical cancer cases in India.

The identification of most common HPV types as etiological risk factors for cervical cancer has led to the development of prophylactic vaccines against specific sets of HPV genotypes. Two prophylactic HPV vaccines are now available in the Indian market for preventing HPV infection and thereby reduce the risk of cervical cancer in women (Gardasil<sup>®</sup> and Cervarix<sup>®</sup>). These vaccines have been licensed in more than 120 countries for use in control of cervical cancer and 63 countries have also included HPV vaccination to girls in their national immunization programmes.

In India, HPV vaccines were licensed by Drug Controller General (DCGI) to be marketed in the country in 2008/09 on the basis of obligatory clinical trials in the country. Since the approval of DCGI, the HPV vaccines have undergone two major trials in the country. A demonstration (post-licensure) project on the HPV vaccination by PATH and ICMR in Andhra Pradesh and Gujarat (2009-2010; 24000 girls) and another is an ongoing multi-centric trial on quadrivalent HPV vaccine by

IARC (WHO), Lyon, France, across 6 states at 9 different sites (20000 girls of 10-18 yrs; since 2009), which has shown very positive and promising results with regard to high acceptance of HPV vaccination by parents of girls, safety, immunogenicity and also efficacy of 2-dose being comparable to 3-dose regime (unpublished data).

In view of the positive field results from clinical and demonstration trials, it was expected that the licensing of HPV vaccines in India (a country with reported high rates of incidence and mortality of cervical cancer) would allow vaccination to become a preferred method of primary prevention of cervical cancer supplementing the proposed population-based screening programmes in the country. However, due to the death of a few girls among vaccinated cohort and alleged gross irregularities in the methodology of the demonstration (post-licensure) project by PATH/ICMR, the vaccines earned negative publicity in the media. This resulted into the suspension of all ongoing trials on vaccine with the appointment of an Expert Enquiry Committee by Govt. of India in April 2010 to look into the causes of the mishap. The said committee submitted its report in April 2011 to the Government stating that the reported deaths of the vaccinated girls were in no case related to the vaccine in the study.

Nevertheless, due to a continued tirade in the media against the vaccine and persistent silence in the matter from the Govt. of India created huge misgivings and misperception among the parents of girls as well as medical practitioners with regard to the safety of the vaccine as such. This has not only led to the decreased uptake of HPV vaccine in private health sector but also shown unwillingness in country's policy makers for its introduction in the public health care system.

It therefore, became imperative that an extensive advocacy and sensitization programme of medical specialists and those involved in health care policy development at the state and national level be carried out to appraise them with current scientific data on HPV vaccine and its importance in primary prevention of cervical cancer.

Keeping these objectives in view, 3 meetings at different locations in India were organized by Cancer Foundation of India. The venues of meetings were chosen mainly in the states where cervical cancer screening had been initiated as part of public health programme and probability of including HPV vaccination among girls looked more likely, such as the state of Sikkim (Gangtok) and Tamil Nadu (Chennai). Delhi was chosen a venue mainly to address to policy makers at the Central Govt. and others who influence the policy decisions at the central level.

## MEETING AGENDA AND RESOURCE PERSONS

### 1. HPV Vaccine and Cervical Cancer Prevention

GANGTOK (Sikkim), July 5, 2014 at Hotel Mayfair

**Chief Guest: Dr. Kumar Bhandari**

*DG cum Secretary*

*Department of Health Care, Human Services and Family Welfare, Govt. of Sikkim*

#### ➔ Cervical Cancer Prevention and the Role of HPV Vaccine

**Dr. Partha Basu**, *Head, Gynecologic Oncology, Chittaranjan National Cancer Institute, Kolkata*

*(Presentated by Prof. Neerja Bhatla in the absence of Dr. Basu)*

#### ➔ HPV Vaccine trials – Results from International Studies

**Dr. Smita Joshi**, *Hirabai Cowasji Jehangir Med. Res.Ins. & Jehangir Clinical Dev.Centre, Pune*

#### ➔ HPV Vaccine trials - Results from India

**Prof. Neerja Bhatla**, *Dept. of Obs & Gyn., All India Institute of Medical Sciences, New Delhi*

#### ➔ HPV Vaccination in Asia, Africa and Latin America - Relevant leads for India

**Dr. R. Sankaranarayanan**, *International Agency for Research on Cancer (WHO), Lyon, France (An Audio-Visual Presentation)*

#### ➔ Panel discussion on Relevance of HPV Vaccine in India

Moderator: **Prof. Neerja Bhatla**, *Dept. Obs & Gyn., AIIMS, New Delh*

Panel: **Prof. G.K.Rath**, *AIIMS, New Delhi*, **Prof. R.Mehrotra**, *Director, ICPO, Noida*,

**Dr. Smita Joshi**, *HCJMRI & JCDC, Pune*, **Dr. Yogesh Verma**, *STNM Hospital, Gangtok*,

**Dr. Eric Zomawia**, *Govt of Mizoram, Aizawl*

### 2. Recent Advances in Cervical Cancer Prevention

NEW DELHI, November 14, 2014 at Taj Vivanta Ambassador Hotel

**Chief Guest: Dr. Jagdish Prasad**

*Director General of Health Services, Government of India  
Ministry of Health & Family Welfare, New Delhi*

**Guest of Honour: Dr. Ajay Khera**

➤ **Comparative Efficacy of Screening Methods for Cervical Cancer**

*Dr. Partha Basu, Head, Gynecologic Oncology, Chittaranjan National Cancer Institute, Kolkata*

➤ **Strategic Planning of Cervical Cancer Prevention in India**

*Dr. Suchitra Pandit, President, Federation of Gynecological Societies of India (FOGSI)*

➤ **Cervical Cancer Prevention: Looking to the future**

*Dr. Pakhee Aggarwal, Consultant, Obs & Gynecology, Fortis Hospital, New Delhi*

➤ **HPV vaccination and Primary Prevention of Cervical Cancer**

*Dr. Smita Joshi, H.Cowasji Jehangir Med. Res.Ins. & Jehangir Clinical Dev. Centre, Pune*

➤ **HPV Vaccines: Evidence from Clinical Studies from India**

*Prof. Neerja Bhatla, Dept. Obs & Gyn., All India Institute of Medical Sciences, New Delhi*

➤ **Current Global Outlook of HPV Vaccination**

*Dr. Jerard M Selvam, Programme Officer, Non-Communicable Diseases, Department of Health, Tamil Nadu, Chennai*

**3. HPV Vaccine for Primary Prevention of Cervical Cancer**

**CHENNAI** (Tamil Nadu), December 9, 2014 at Taj Vivanta-Connemara Hotel

**Chief Guest: Padmabhushan Prof. Dr. V. Shanta**

*Executive Chairman  
Cancer Institute (WIA), Chennai*

**Guest of Honour: Mr.M.S. Shanmugam, IAS**

*Project Director,  
Tamil Nadu Health Systems Project,  
Government of Tamil Nadu, Chennai*

➤ **HPV Vaccine and Prevention of Cervical Cancer**

*Prof. Shalini Rajaram, Deptt. of Obs & Gyn, Guru Tegh Bahadur Hospital and UCMS, Delhi*

➤ **HPV Vaccine Studies - Results from India**

*Prof. M R Pillai, Director, Rajiv Gandhi Centre of Biotechnology, Thiruvananthapuram*

➤ **HPV studies from India**

*Prof. T. Rajkumar, Head, Deptt. of Molecular Oncology, Cancer Institute (WIA), Chennai*

➤ **HPV Vaccination - Global Outlook**

*Dr. Partha Basu, Head, Gynecologic Oncology, Chittaranjan National Cancer Institute, Kolkata*

➤ **Prospects and Prejudices of HPV Vaccines in India**

*Prof. Ravi Mehrotra, Director, Institute of Cytology & Preventive Oncology (ICMR), Noida, U.P.*

**CHAIRPERSONS** (at Gangtok, Delhi and Chennai meetings)

- **Prof. G.K.Rath**, Chief, Dr BRA Institute Rotary Cancer Hospital, AIIMS, New Delhi
- **Prof. Ravi Mehrotra**, Director, Institute of Cytology & Preventive Oncology (ICMR), Noida, U.P
- **Prof. Maqsood Siddiqi**, Chairman, Cancer Foundation of India, Kolkata
- **Dr. Rupinder Sekhon**, Sr. Consultant, Rajiv Gandhi Cancer Institute & Res. Centre, New Delhi
- **Prof. Alka Kriplani**, Head, Dept. Obs & Gyn., All India Institute of Medical Sciences, New Delhi
- **Dr. D.K.Shukla**, Head, Division of NCD, Indian Council of Medical Research, New Delhi
- **Dr. Tanvir Kaur**, Division of NCD, Indian Council of Medical Research, New Delhi
- **Prof. B.C. Das**, Former Director, ICPO (ICMR) and Amity University, Noida, U.P
- **Dr. Ajay Khera**, DC, Ch & Immunization, National Health Mission, Govt. of India, New Delhi
- **Dr. Bhadrasain Vikram**, Chief, Clinical Radiation Oncology, National Cancer Institute, USA
- **Prof. V Sridevi**, Head, Deptt. Of Surgery, Cancer Institute (WIA), Chennai
- **Prof. Priya Abraham**, Head, Deptt. Of Clinical Virology, Christian Medical College, Vellore
- **Prof. Shalini Rajaram**, Deptt. Of Obs & Gyn, Guru Tegh Bahadur Hospital and UCMS, Delhi
- **Dr. R. Swaminathan**, Head Deptt of Epid.& Biostatistics, Cancer Institute (WIA), Chennai
- **Dr. Jerard M Selvam**, Programme Officer, Non-Communicable Diseases, Department of Health, Tamil Nadu, Chennai

## PARTICIPANTS

### GANGTOK, July 5, 2014

- **Govt. Representatives from NE States:** Representatives from the states of Arunachal Pradesh, Manipur, Meghalaya, Mizoram, Nagaland, and Tripura.
- **Govt. of Sikkim:** 16 high ranking officials from Department of Health Care, Human Services and Family Welfare including Health Secretary and Director, NHM
- **Academia:** Sikkim Manipal Institute of Medical Sciences, Gangtok

### DELHI, November 14, 2014

- **Govt. of India Representatives:** Director General of Health Services, Govt of India, MOHFW and DC of Child welfare and Immunisation programme, National Health Mission, MOHFW.
- **Representatives from related Govt. Departments:** Department of Health Research (DHR), ICMR, DBT.
- **International Health Organisation:** WHO India office, US Embassy, New Delhi, NCI
- **NGOs:** Cansupport, Public Health Foundation of India, Population Service International, Research Triangle Institute, Global Health Strategies,
- **Academia:** Hamdard University, Amity University, Noida

### CHENNAI, December 9, 2014

- **Govt. of Tamil Nadu representatives:** Project Director, TN Health Systems Projects and Deputy Director & State Programme Officer - NCD
- **Representatives from:** Cancer Institute (WIA), CMC, Vellore, Meenakshi Medical Centre, Kancheepuram,
- **NGOs:** Canstop, Christian Fellowship Community Centre, Ambilikkai, Jeevodaya, Karnataka Health Promotion Trust, Bangalore.

## SUMMARY OF PRESENTATIONS

Summary of selected presentations is given below in order to avoid repetition of subject content

|                             |   |
|-----------------------------|---|
| <b>Welcome to Delegates</b> | <b>Prof. Maqsood Siddiqi</b><br>CHAIRMAN<br>Cancer Foundation of India (CFI), Kolkata |
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Prof. Siddiqi welcomed the delegates on behalf of Cancer Foundation of India (CFI), at all the 3 venues of the Symposia. While welcoming the delegates in Gangtok, he stated that these meetings are being organized to *“provide a common forum to bring various stakeholders involved in search of methods and appropriate logistics for an effective cervical cancer control programme in the country. The stakeholders include the health care expert involved in policy development, those generating information on risk factors of the disease, the implementation scientists associated with the prevention in control and those who facilitate the capacity building of human resource required for countrywide prevention programme on cervical cancer”*.

In the meeting at Delhi he said that an *“important aim of today’s meeting is to discuss some of the new results emerging from HPV vaccination trials in India as well as the universal verification of its safety and efficacy in primary prevention of cervical cancer. While a few state governments in the country have initiated population based cervical cancer screening among adult women and more are likely to follow, the CFI strongly feels that it is time that the government should have a fresh look on the question of introducing HPV vaccination of girls under the public health care delivery system”*. He further pleaded with the DGHS who was present in the meeting being the Chief Guest, that *“In view of more than 120 countries having approved the vaccine and more than 60 countries where HPV vaccination has been included in their national immunization agenda...it is time we adopt more proactive and pragmatic approach towards prevention of cervical cancer and take necessary steps to include HPV in universal immunization programme at least in the states who wish to undertake with their own resources”*.

Prof. Siddiqi also assured the participants in Chennai meeting that the fears created by the media on the safety of HPV vaccines *“due to the death of few girls among vaccinated cohort in the demonstration project by Path / ICMR in Andhra Pradesh and Gujarat”* have been negated by the *“Government of India appointed expert committee which did not find any relation of HPV vaccine with the reported deaths in the study”*.

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| <b>Guest of Honour</b><br>(Delhi, November 9, 2014) | <b>Dr. Ajay Khera</b><br>DC, Child Health & Immunisation<br>Govt. of India, Ministry of Health and Family Welfare,<br>New Delhi |
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Dr Khera began his address by extending a *“very warm welcome to all of you, on behalf of the Ministry of Health and Family Welfare”* and expressed his appreciation *“for organizing such an important meeting”*. He described the success of National Health Mission programme as well as the universal immunization programme which has resulted in *“improving the child survival as well as the (reduction in) maternal mortality”* in the country. Dr. Khera while discussing the possibility of introducing HPV vaccine in the UIP said *“today our UIP programme is Child centric program. It basically tries to address the issues around child mortality that’s why you find most of the our UIP vaccines are focused around child under 5, but I think it is high time that we need to talk about a kind of vaccine in a life cycle approach may be the vaccine in the adolescents, even the vaccine in the elderly population and I think there has been a lot of discussion happening around it, and HPV vaccine could be one of the potential candidates in coming days when we will talk about the adolescent health or when we talk about improving the school health system in the country”*.

He also expressed hope that *“we should be able to take the agenda of HPV vaccine at right place through the system of NTAGI and then it may be in the coming years, you know, (it may) become a universal programme”*.

**Chief Guest**

(Delhi, November 9, 2014)

**Dr. Jagdish Prasad**

Director General of Health Services (DGHS)

Govt. of India, Ministry of Health & Family Welfare New Delhi

Dr. Prasad began his address by describing the problems of NCD globally as well as in India. With regard to the burden of cervical cancer he said *“today, the cervical cancer is the 2<sup>nd</sup> most common killer for women after breast cancer. All of you are well aware that in the whole world we have more than 5,27,000 new cases per year of cervical cancer and 2,27,000 patients die each year. And if you consider the Indian burden, of the 1,20,000 cervical cancer each year, about 70,000 patients die, which is a huge number and the 5 year survival is not more than 50%...so the time has come to realize that the cost of the prevention is hardly anything compared to the treatment cost and the life of the patient”* He talked of a forthcoming meeting of Government of India formed committee of gynaecologists where the question of HPV vaccine will be discussed.

Dr Prasad very candidly touched upon the HPV vaccine controversy and said *“and we know that a question was raised by a Member of Parliament that cervical cancer vaccine is causing some problem but when we got it investigated by the ICMR it was found that it is false. It was not because of the cervical cancer vaccine, it was something else”*. Dr. Prasad, next made the most important statement on HPV vaccine, almost amounting to a policy announcement that ***“recently as a technical adviser to the Government of India, I have permitted the Sikkim government (that) they can give the vaccine to (girls in) their own state”***. He further stated that ***“I have also taken the technical decision that any state which asks me for the permission (will get it) because all of us know that in private sector they (are) already using the vaccine”***.

While underscoring the commitment of Government of India in controlling cervical cancer, he discussed the programme under which cervical screening has begun in 100 districts in the country and more districts are to be added soon. He invited NGOs, Gynaecologists FOGSI to come forward and help the government in cervical cancer screening by stating *“I want that you people organize and tell us that you adopt one district or even half district, even 5 lakh population and that you’d do the screening for us and it will be helpful for people (and) also for the country”*. With this Dr. Prasad again highlighted that HPV vaccine can be introduced by states at their cost by stating that *“the Government of India will take time to put it in Universal Immunization Programme, but if the states who have money can use the vaccination, we have no problem”*.

In the end Dr. Prasad expressed hope that *“this symposium will give some feedback to Government of India to take further steps”*.

| TOPIC   | SPEAKER   | CHAIRPERSON  |
|---|---|--|
| <b>HPV Vaccines: Evidence from Clinical Studies in India</b><br>(Gangtok, July 5, 2014) | <b>Prof. Neerja Bhatla</b><br>Dept. Obs & Gyn.,<br>All India Institute of Medical Sciences, New Delhi | <b>Prof. G.K.Rath</b><br>Chief, Dr BRA Institute<br>International Rotary Cancer Hospital, AIIMS, New Delhi |

Prof. Bhatla made a comprehensive review of HPV infection epidemiology and type distribution in India. Presenting results from her own research group and collaborators, she emphasized that 84.1 % of cervical cancers can be prevented through HPV vaccination in India as against commonly believed estimate of only 70%. She presented results from a multi-centric study on bivalent vaccine among healthy Indian women, showing good acceptance and compliance, safety and immunogenicity. Prof. Bhatla also described the results from a large demonstration project (2009-2010; 24,000 girls) in Khammam district of Andhra Pradesh and Vadodra district in Gujarat on girls aged 10-13 yrs showing a high 3-dose compliance (89.9 and 78.1 % respectively) and positive acceptance of HPV vaccination by parents of girls with the understanding that the vaccine protects from cervical cancer. Non-acceptance was mainly for the lack of education about the programme. Preliminary results from another major multi-centric trial of HPV vaccine in India (20,000 girls, age 10-18 yrs), the 2 dose-vs-3 dose trial by IARC (WHO) on quadrivalent vaccine were also discussed in detail. Despite suspension of the project mid-way due to ICMR's order, early results from the trial evidently show that all doses are immunogenic and levels after 36 months are several-fold higher than natural infection. The frequency of HPV type 16/18 in 3 dose vaccinated girls was 0.8 % compared to 2.7 % in unvaccinated girls. The study also shows that the 2-dose vaccination regime is comparable to immunogenic response of the 3-dose regime. In conclusion, Prof Bhatla advised that along with secondary prevention, HPV vaccination is an important complimentary strategy for prevention of cervical cancer in the country. To achieve this, however, the misconceptions and misperceptions must be cleared and awareness is improved among common people, she added.

| TOPIC  | SPEAKER  | CHAIRPERSON   |
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| <b>HPV Vaccine Trials: Results from International Studies</b><br>(Gangtok, July 5, 2014) | <b>Dr. Smita Joshi,</b><br>Hirabai Cowasji Jehangir Med. Research Institute & Jehangir Clinical Dev.Centre, Pune | <b>Prof. Maqsood Siddiqi</b><br>CHAIRMAN<br>Cancer Foundation of India (CFI)<br>Kolkata |

Dr. Joshi began her lecture by presenting the background information on HPV vaccine, its production using DNA recombinant technology and the proposed mechanism of protection it provides from infection. She followed it up with a detailed description of the results from the well known FUTURE I, FUTURE II, PATRICIA and Costa Rica trials on the efficacy and safety of quadrivalent and bivalent HPV vaccines – the immune response results of these vaccines and the immuno bridging studies between different age groups of girls and women. She also discussed the studies on quadrivalent vaccine which showed its efficacy in women aged 24-45 yrs who were not infected with relevant HPV types at enrolment. She apprised the audience with Costa Rica trials and those in Canada and Germany which showed HPV vaccine efficacy of fewer than 3 doses by demonstrating antibody response in 2 dose comparable to 3 dose vaccine up to 4 years. She also talked of SAGE (WHO) recommendations that 2 dose vaccine at an interval of 6 months can be given to girls below 15 yrs, while 3-dose regimen be continued in cases of girls above 15 yrs and in immune-compromised girls. Dr. Joshi presented results of HPV vaccine on HIV infected girls showing that HPV vaccine is safe and immunogenic in such cases. A recent report from US National Health and Nutrition Survey was cited showing a drop in prevalence of HPV infection among girls of 14-19 yrs of age from 56 % in 2003-06 to 5.1 % in 2007-10. She validated her support for HPV vaccination by referring to the results from long-term follow up studies of about 10 yrs showing that antibody titre against HPV 16 and 18 VLP remained several fold higher above natural infection level in vaccinated individuals. Dr. Joshi concluded her talk by stating that 217,786 girls have received vaccination in 14 countries under 21 school and health-clinic-based programmes under Gardasil Access scheme between 2009 and 2013.

| TOPIC   | SPEAKER  | INTRODUCED BY   |
|---|--|---|
| <b>HPV vaccination in Asia, Africa and Latin America – <i>Relevant leads for India</i></b><br>(Gangtok, July 5, 2014) | <b>Dr. R. Sankaranarayanan,</b><br>International Agency for Research on Cancer (WHO),<br>Lyon, France<br><b>(Video recorded Lecture)</b> | <b>Prof. Maqsood Siddiqi</b><br>CHAIRMAN<br>Cancer Foundation of India (CFI)<br>Kolkata |

Dr. Sankaranarayanan while describing the high incidence and mortality rates of cervical cancer in India expressed his disappointment over the laid-back approach towards its prevention strategy in the country. He articulated his view by showing data where some of the small countries in Africa, Asia and Latin America have initiated national programmes of screening and HPV vaccination for prevention of the disease. He outlined the risk factors for cervical cancer and highlighted the primary prevention through HPV vaccination. He described in detail the 62 countries where HPV vaccination has been included in their national immunization agenda. Dr. Sankaranarayanan was categorical in asking as to why India is not stepping ahead with nation-wide primary and secondary prevention programme of cervical cancer when Asian and African countries like Bhutan, Malaysia and Rwanda have gone ahead with HPV vaccination and screening successfully since 2009/2010. He described in detail the vaccination programme in Malaysia and expressed appreciation of the firm and pragmatic stand taken by its government despite anti-vaccine movements similar to what we have in India. Dr. Sankaranarayanan presented results from IARC multi-centric trial on HPV vaccine in India (2 dose-vs-3 dose trial since 2009) which shows highly promising results with regard to safety, immunogenicity and efficacy of 2-dose being comparable to 3-dose regime. On the basis of results from various trials globally where similar results were obtained by default, 7 countries have included 2-dose regime in their national immunization programme. He referred to the Australian vaccination programme since 2007 which is already showing decline in cervical cancer incidence. Finally, he advised that in view of the available international and national evidence, it would be highly rational and pragmatic for India to start HPV vaccination for girls of 9-13 yrs of age along with population-based screening using HPV detection method for women above 35 yrs in its cervical cancer prevention programme.

| PANEL DISCUSSION ON   | MODERATED BY   |
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| <b>Relevance of HPV vaccine in India</b><br>(Gangtok, July 5, 2014) | <b>Prof. Neerja Bhatla</b><br>Dept. Obs & Gyn.<br>All India Institute of Medical Sciences, New Delhi |

Panelists:

**Prof. G.K. Rath** of AIIMS, New Delhi, **Prof. Ravi Mehrotra**, ICPO (ICMR), Noida

**Dr. Smita Joshi**, JCDC, Pune, **Dr. Eric Zomawia**, Govt. of Mizoram, Aizawl and

**Dr. Yogesh Verma**, Medical Superintendent, STNM Hospital, Gangtok.

Prof. Bhatla requested each panelist to speak on the following topics and invited comments and questions from the audience. The topics were, Cervical Cancer – Magnitude of the problem, trends in cervical cancer incidence, implication of prevention programs in India. **(GKR)**, Methods for cervical cancer prevention. What are our choices? **(SJ)**, why did screening take so long to set up? Will it ever succeed **(RM)**. Need for HPV vaccination, **(YV)**. What are the presently accepted schedules? **(EZ)**, which age group/s? **(YV)**, what are the expected barriers and do we have solutions? **(EZ)**, Advantages of implementing 2-dose regimes? **(SJ)**, what will be the place of screening after HPV vaccination programs are in place? **(RM)**, which is more cost-effective, screening or vaccination? **(YV)**, which diseases will be prevented by HPV vaccination? **(GKR)**. HPV vaccination in males, help or hindrance? **(SJ)**.

The short discourse by each panelist attracted comments from the participants in the meeting and resulted into a stimulating discussion covering a whole range of constructive and positive suggestions on the possibilities of launching cervical cancer prevention programmes in the country and particularly in NE states. While there was general agreement that sufficient background information is now available on the feasibility of a successful population-based HPV vaccination and screening of women to prevent cervical cancer in the country, suggestions were made by the participants which need to be simultaneously addressed with respect to the logistics of cold chain, challenges of compliance to multi-dose vaccination, socio-cultural barriers for screening of women, appropriate communication material for educating women and more importantly cost-effectiveness of screening and vaccination as a public health measure in India.

| TOPIC  | SPEAKER  | CHAIRPERSON   |
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| <b>Comparative Efficacy of Screening Methods for Cervical Cancer</b><br>(Delhi, November 14, 2014) | <b>Dr. Partha S. Basu</b><br>Head, Dept. of Gynecologic Oncology,<br>Chittaranjan National Cancer Institute, Kolkata | <b>Dr. Rupinder Sekhon</b><br>Senior Consultant<br>Gynecologic Oncology.<br>Rajiv Gandhi Cancer Institute &<br>Research Centre, Delhi |

While HPV vaccination has emerged as preferred method for primary prevention of cervical cancer, the cervical screening of adult women would remain the core method of detection and treatment of pre-invasive and invasive cervical lesions. Dr Basu presented an excellent review on the efficacy of different methods of cervical screening. He initiated the discussion with analysis of Pap test (Papanicolaou Test) and its success in reducing the incidence and mortality (50 – 70 %) of cervical cancer in U.K. and North America. He however mentioned that when the Pap test was used for screening in Latin America and Sri Lanka, no reduction in mortality rates were observed. He attributed this to a low Sensitivity or efficiency of Pap test in picking up positive cases (20-60%) due to which repeated screening is needed as practiced in the West and is not possible in low resource countries. Dr. Basu then reviewed the work on VIA test (Visual inspection using Acetic acid) and termed it to be logistically suitable and most cost effective method for screening women in low resource countries for various reasons including that the test could done by trained nurse or even a health worker and is more sensitive than Pap test.

Since it is now well established that Human Papilloma virus (HPV) is a necessary cause of cervical cancer, Dr. Basu discussed data on the use of Hybrid Capture II test (HC-II) measuring DNA of 13 oncogenic HPV types, as a screening tool. The HC-II test shows a Sensitivity of more than 90 %. The cluster-randomized control study of Dr.Sankarnarayanan et al. in Barshi, Maharashtra, was described in detail where a comparison was made between VIA, Cytology (Pap test) and HC II test on 131,746 rural women of 30 – 59 yrs. Each test group consisted of more than 30,000 women. The hazard ratio for the detection of advanced cancer (stage II+) in the HPV-testing group was, 0.47 as compared to 0.75 and 1.04 in Cytology and VIA group respectively. The hazard ratio of Death from cervical cancer was 0.52 in HC II, 0.89 in cytology and 0.86 in VIA compared to 1.0 in control group showing a reduction of 50 % in mortality rates among women who were screened by HC II test, and no significant reductions were observed in the cytologic test group or in the VIA group. The described work thus showed that a single round of HPV testing significantly reduced the numbers of advanced cervical cancers and mortality from the disease.

Dr. Basu then discussed in detail his own recent work from a demonstration project in rural Bengal where 39,740 women were screened using HC II and VIA test to compare their accuracies in a population setting. The screen positivity was 7.1% for VIA and 4.7% for HC II, whereas the detection rate of CIN 3+ disease was significantly higher with HC II than VIA, 3.8 and 2.8 respectively. Sensitivities of VIA and HC II to detect 162 histology proven CIN 3+ lesions were found to be 67.9 and 91.2%, and specificities were 93.2 and 96.9 respectively. He therefore, recommended that triaging of VIA positive women with HC II test would considerably improve the positive predictive value of detecting CIN 3+ from 4.0 to 37.5 %. His work further demonstrated that screen positive women with follow up of colposcopy resulted in significant down-staging of cancer and more cancer were detected in stage I.

| TOPIC  | SPEAKER   | CHAIRPERSON  |
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| <b>HPV Vaccine and Prevention of Cervical Cancer</b><br>(Chennai, 9 December 2014) | <b>Prof. Shalini Rajaram</b><br>Director Professor, Obstetrics & Gynaecology,<br>Guru Teg Bahadur Hospital and UCMS, Delhi, | <b>Prof. V. Sridevi</b><br>Department of Surgical Oncology, Cancer Institute (WIA), Chennai. |

Prof. Shalini first described the epidemiology of cervical cancer in India and attributed the reported decrease in incidence of the disease mainly to changing life style and literacy among women. Although agreeing with the necessity of population based cervical screening of 30+ women and its cost effectiveness, she expressed her reservation on the logistics of its implementation and the motivation of women to come for screening. She described the work in Australia where after implementation of nation-wide HPV vaccination programme, there is significant decrease in women seeking invasive procedures like LEEP, cryotherapy and colposcopic biopsy. Prof. Shalini strongly recommended the inclusion of HPV vaccine for 9-13 yrs old girls in the UIP, referring to the acceptance of HPV vaccination by Indian Academy of Pediatrics (IAP) and FOGSI. As regards the high cost of vaccine, she recommended that the government of India should avail the facility under GAVI to receive each dose of vaccine at US\$ 5, as has been done in many low and middle income countries to initiate HPV vaccination programmes.

Prof Shalini then presented the background information on the structure of HPV and molecular mechanism of its infection before discussing the production of vaccine using recombinant technology and prevention of HPV infection by the prophylactic HPV vaccine. She followed it up with a detailed description of the Phase III efficacy and safety studies, immunobridging and 2-dose/3-dose Costa Rica studies. In conclusion, Prof. Shalini emphatically stated that

HPV vaccines are safe with no causal relationship with the SAEs, these are highly immunogenic and sustained serum antibody responses for years, provide partial cross-protection against phylogenetically-related non-vaccine types and stated that to date there are no signs of waning protection.

## WHAT THE EXPERTS SAID – QUOTABLE QUOTES

### **On HPV vaccination**

“The government is also aware of the fact that a good and effective vaccine that is HPV vaccination is available and can be very useful in prevention of cervical cancer if administered in the proper stipulated time”.

**Dr. Kumar Bhandari**

*DG cum Secretary*

*Department of Health Care, Human Services  
and Family Welfare, Govt. of Sikkim, Gangtok*

“HPV vaccination is an important complimentary strategy. Formative studies and demonstration studies have documented good acceptability and feasibility. The 2 dose regimens have great potential to decrease cost and improve compliance but misconceptions must be cleared and awareness improved among the population at large”.

**Prof. Neerja Bhatla**

*Dept. Obstetrics & Gynecology,*

*All India Institute of Medical Sciences, New Delhi*

“The already conducted clinical trials indicate that HPV vaccine is safe and it is efficacious in preventing HPV infection in HPV naïve women and it prevents HPV 16 & 18 related cervical pre-cancer lesions.....The vaccines are well accepted and they do not result in severe adverse events such as death which are attributable to vaccination and they are safe”.

“There is a pressing need in India to introduce cervical cancer control measures as India is the largest contributor of cervical cancer burden in the world”.

**Dr. R. Sankaranarayanan,**

*International Agency for Research on Cancer (WHO), Lyon, France*

“FOGSI tries to help in various government programmes. We try to integrate the reproductive health services for empowering adolescents with information about primary cervical cancer prevention..... We have a very encouraging feedback from students and currently we have sensitized over 40000 students and we have vaccinated about 10,000”.

**Dr. Suchitra Pandit,**

*President,*

*Federation of Gynecological Societies of India (FOGSI)*

“When it comes to the HPV vaccine, besides targeting the young people you have to target the parents because most of the misgivings, I find people I speak to, come from the parents and sometimes from the women in the household”.

**Ms. Harmala Gupta**  
*Cansupport, New Delhi*

“Cancer Foundation of India very strongly feels that it is time that the government should have a fresh look on the question of introducing HPV vaccination of girls under the public Health care delivery system”.

**Prof. Maqsood Siddiqi**  
*Chairman,  
Cancer Foundation of India, Kolkata*

“HPV vaccine could be one of the potential candidates in coming days when we will talk about the adolescent health or when we talk about improving the school health system in the country”.

**Dr. Ajay Khera**  
*DC, Ch & Immunization,  
National Health Mission, Govt. of India, New Delhi*

“I am with you people and I think that the vaccine will be earliest to be put in UIP but any state asking me as a technical adviser, I am telling them to use the vaccine”.

**Dr. Jagdish Prasad**  
*Director General of Health Services,  
Government of India  
Ministry of Health & Family Welfare, New Delhi*

“In primary prevention, we have to think about the vaccination for HPV and good ages are 9 to 13 years, 10 years onwards yes, and a good sound IEC, sexual health education which focuses especially the school children, the adolescents who will be in the school that time”.

**Dr. Jerard M Selvam**  
*Programme Officer,  
Non-Communicable Diseases,  
Department of Health, Tamil Nadu, Chennai*

“HPV prevalence rate does seem to be varying in different parts of the country, However 16 & 18 types still predominate and this is something which is striking and the uniform prevalence rate across different age group”.

**Prof. T. Rajkumar,**  
*Head, Deptt. of Molecular Oncology,  
Cancer Institute (WIA), Chennai*

“Why should we do a secondary prevention, why should we wait for changes to occur and then pick it up and prevent cervical cancer from occurring? Yes this may be cost effective but...we need to look into more cost effective vaccines, less expensive vaccines which we should be working on.

**Prof. Shalini Rajaram**  
*Deptt. of Obs & Gyn, Guru Tegh Bahadur Hospital and UCMS, Delhi*

## **On Cervical Screening**

“Cervical Cancer continues to be a major problem and we have no effective national programme possible for cervical cancer screening, the coverage has been abysmally poor 5% in urban and 2% in rural areas. Addition of HPV vaccine will lead to comprehensive cervical cancer control with additional protection against other diseases as well”.

**Prof. Neerja Bhatla**

*Dept. Obstetrics & Gynecology,  
All India Institute of Medical Sciences, New Delhi*

“A simple integration of vaccinating 11 or 12 year old girls and providing a single HPV screen at age 35 for example could be a very pragmatic way of preventing substantial cervical cancer burden in low and middle income countries in a cost-effective manner”.

**Dr. R. Sankaranarayanan,**

*International Agency for Research on Cancer (WHO), Lyon, France*

“Choose whatever method suits, it may be VIA or it may be HPV testing, but make a beginning. What is important is to develop the infrastructure. The infrastructure of recalling women, for treatment of screen detected positive cases, and the monitoring of the programme”.

“Cervical cancer screening is one of the most cost effective health interventions almost as cost effective as providing clean water to prevent diarrheal diseases”.

**Dr. Partha Basu,**

*Head, Gynecologic Oncology,  
Chittaranjan National Cancer Institute, Kolkata*

“This is a World Bank funded project and this (cervical screening) is one of the core activity under the project....The screening has been very promising. However, we have challenges and concerns in the field of follow-up of the screened positive patients. We have so far screened 67,00,000 women in Tamil Nadu in the target age population of 30-60 and the positivity rate was 3.87 which is 2.62 lakh people found positive in the initial screening”

**M.S.Shanmugam, IAS**

*Project Director,  
Tamil Nadu Health Systems Project,  
Government of Tamil Nadu, Chennai.*

“Vaccination programme should follow effective screening programme to start with. We cannot start up vaccination program without an effective screening programme it can be parallel after sometime, after we have an established a good screening programme then probably it can become parallel”.

**Padmabhushan Prof. Dr. V. Shanta**

*Executive Chairman  
Cancer Institute (WIA), Chennai*

## KEY MESSAGES AND RECOMMENDATIONS

The 3 roundtables provided a unique opportunity to 24 experts of preeminence in the field of cervical cancer prevention and public health to deliberate on the Indian and global data on HPV vaccination of girls and cervical screening of women in the context of cervical cancer control in India. The discussions were enriched with the presence of more than 110 invited stakeholders representing policy makers from central and state governments, national and international NGOs and specialists from leading medical institutions in the country. The deliberations greatly helped in putting the relevance and importance of HPV vaccination in right perspective before the participants including the policy makers. There were also stimulating discussions on recent results from India on the efficacy of different methods of cervical screening.

As an outcome of the roundtables several important messages and recommendations have emerged to develop a comprehensive strategy to prevent and control cervical cancer incidence and mortality rates in India. The key messages and recommendation are listed below.

### ➤ ***A comprehensive cervical cancer programme must have the following components:***

- ✓ *Educating women on the risk of the disease using appropriately designed communication material*
- ✓ *HPV vaccination of 9-13 yrs old girls with proper consent of their parents*
- ✓ *Develop population based cervical screening programmes with high coverage for 30+ women using VIA and/or HC II tests*
- ✓ *Cervical screening of women must be linked to treatment.*

### ➤ ***HPV vaccination to 9-13 yrs old girls is an effective and safe method for primary prevention of cervical cancer in India***

- ✓ *HPV vaccines are safe with no causal relationship with the SAEs. These are highly immunogenic and sustained serum antibody responses for several years and provide partial cross-protection against phylogenetically-related non-vaccine types.*
- ✓ *Since more than a 120 countries have licensed HPV vaccine and more than 170 million doses have been administered worldwide, the safety of the vaccine is already established.*

- ✓ *The vast majority of suspected AEs are related to recognized side effects already listed due to the injection process itself and no serious new risks have been identified due to HPV vaccine.*
- ✓ *HPV vaccination is recommended by Indian Academy of Pediatrics (IAP) and FOGSI.*
- ✓ *HPV vaccine has been shown to be culturally acceptable by large populations in the country as evidenced by the demonstration trial involving about 24,000 girls in Andhra Pradesh and Gujarat (2009-2010) and the 2-vs-3 dose trial on diverse population of about 20,000 girls in multi-centre study in 7 states (2009-2015).*
- ✓ *Government of India should consider availing the facility under GAVI to receive each dose of HPV vaccine at US\$ 5, as has been done in many low and middle income countries.*

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