THE QUATERELY E-NEWSLETTER SEPT. 2017

AOGIN INDIA

Vol.4 No.3 September 2017

Asia Oceania research organization on Genital Infections and Neoplasia–India

Office Bearers

- **Founder President**
  Neerja Bhatla
- **Past president**
  Partha Basu
- **President**
  Shalini Rajaram
- **Vice President**
  Abraham Peedacayil
- **Secretary**
  Rupinder Sekhon
- **Joint secretary**
  Alok Bharti
  Srabani Mittal
- **Clinical Secretary**
  Bindiya Gupta
- **Treasurer**
  Sabhyata Gupta
- **Editor**
  Nisha Singh
- **Web Editor**
  Dipanwita Bannerjee
- **Executive Committee**
  Indrani Ganguli
  Harsha Khullar
  Kanika Gupta
  Lata Balasubramani
  Sarita Kothari
  Bhagyalaxmi Naik

FROM THE EDITOR'S DESK

Dear AOGIN India members

Heartiest welcome to Lucknow for AOGIN India 2017

You can all imagine the excitement of releasing the print issue of AOGIN India newsletter from Lucknow during AOGIN India 2017! It is really a rewarding experience.

It is an honour to publish articles from international experts including Dr R. Sankaranarayanan from IARC, France, Dr Mona Saraiya from CDC, USA, Dr Ashrafunnesa from Bangladesh, Dr Ricky Lu from JHPIEGO and Dr Niharika Khanna from USA

We are grateful to them for sending writeups for the newsletter. Some of our national experts like Dr SB Khanna, Dr Geetanjali Amin and Dr Puneet Chandna have also contributed articles on HPV vaccine, basics of colposcopy and cancer diagnostics respectively.

I hope you will all enjoy reading the newsletter in the print form.

With best wishes
Prof Nisha Singh
Editor

WHAT'S INSIDE

Current status of HPV vaccination around the world

R. Sankaranarayanan MD

Special Advisor on Cancer Control (CCO)
Head, Screening Group (SCR)

World Health Organization-International Agency for Research on Cancer (WHO-IARC) Lyon, France

Persistent genital tract infections with one of the 14 types of human papillomaviruses (high risk HPV types) cause virtually all cases of cervical cancer. Of the cervical cancer causing HPV viruses, HPV type 16 causes about 50-60% and HPV type 18 accounts for around 15-20% of all cervical cancer cases in different regions of the world. The remaining 12 HPV types account for around 25-30% of cervical cancers. This knowledge has led to the development of HPV vaccination as a major public health strategy for preventing cervical cancer. Currently two commercially available HPV vaccines target to prevent persistent genital tract infections with HPV 16 and HPV 18: a bivalent vaccine (Cervarix) targeting HPV types 16 and 18 and a quadrivalent vaccine (Gardasil) targeting HPV 6 and 11 (which cause genital warts) and HPV 16 and 18. In addition, a 9-valent HPV vaccine (Gardasil 9) targeting HPV types 31, 33, 45, 52 and 58 in addition to HPV types 6,11,16 and 18 has been licensed.

Currently recommended HPV vaccine dose schedules include 2-doses over 6-12 months for persons less than 15 years old and 3-doses over 6 months for those aged 15 years or more and for immunocompromised persons. The World Health Organization (WHO-) recommends a 2-dose schedule for less than 15 year old girls based on the fact that immunogenicity of 2 doses of HPV vaccines are non-inferior to 3-doses in 15-26 year old women. Currently HPV vaccination has been introduced as part of national immunization programs in 72 countries that also includes some LMICs. Among LMICs, the Latin American region is leading in making HPV vaccine accessible to girls aged 9-14 years; as of now 7 out of 8 girls in the Latin American region have access to HPV vaccination through public programs which is a remarkable achievement indeed. The largest HPV vaccination program in LMICs exist in Brazil where more than 5 million girls and boys are targeted annually. On the other hand, the Asian region which contributes major share of global cervical cancer burden substantially lags behind in introducing HPV vaccination in national immunization programs. Currently only Bangladesh, Bhutan, Brunei, Japan, Malaysia, Nepal, Thailand, South Korea, Philippines, United Arab Emirates and Uzbekistan in Asia have introduced HPV vaccination in their national immunization program.

Recently some studies have demonstrated that even a single dose of HPV vaccination is associated with a robust and sustained immune and similar effectiveness in preventing persistent HPV 16 and 18 infection following a single dose of HPV vaccination. A single dose schedule if found effective will have dramatic cost saving and programmatic advantages over two or three doses that will significantly facilitate vaccination introduction and high coverage of target girls globally. However, more robust evidence on long term efficacy in terms of protection against persistent HPV infection as well as additional data confirming the current evidence from a planned randomized trial comparing a single dose with two doses are needed before policy guidelines regarding a single dose can be formulated and implemented.

AOGIN-INDIA Vision Statement

AOGIN India's vision is to reduce the burden of diseases caused by reproductive tract infections, especially Human Papillomavirus (HPV), in India. Furthermore, AOGIN India's mission is to work with governments, non-governmental organizations, learned societies, health care workers and the lay public, to communicate, cooperate and share information in India and neighboring countries pertaining to prevention, early detection and management of cervical cancer and other genital cancers.

Recent changes of Cervical Cancer Screening Programme in Bangladesh

Prof. Ashrafun Nessa
Bangabandhu Sheikh Mujib Medical University
Dhaka, Bangladesh

Cervical cancer is the second-most common cancer among women in Bangladesh. The Government of Bangladesh (GOB) in collaboration with UNFPA and Bangabandhu Sheikh Mujib Medical University (BSMMU) has taken a programmatic approach to develop a cervical cancer screening programme through introducing Visual Inspection of Cervix with Acetic Acid (VIA). A pilot programme to assess the feasibility of VIA in 16 Districts in the year 2005, was followed by expansion of VIA facilities to the remaining 48 districts by the year 2012. Since then, GOB initiated scaling-up the VIA programme towards sub-district (upazila) level. Till date 1895 service providers (358 doctors and 1537 Nurses, FWVs, paramedics) of 411 VIA centres received training and are offering VIA to all ever married women aged 30 years and above. After establishing the VIA centre at each selected upazila, three to four-day long VIA camp is being organized with facilities of awareness creation, counseling and VIA. Since 2005, 160 postgraduate gynaecologists received training on colposcopy. Screen positive cases are being referred to the colposcopy clinics of tertiary level health-care facilities (BSMMU / 14 MCHs) for evaluation and management. 1386807 VIA tests were performed from January 2005 to December 2016 and of them 65747 (4.74%) women were VIA positive. Among them 20776 (31.60%) attended the colposcopy clinic of BSMMU and of them about 52% had precancerous or cancerous conditions of the cervix, 3101 (15%) were treated by LEEP, 2197 (10.60%) by thermo-coagulation and 1155 (5.50%) women with cervical cancer were referred to oncology. In Bangladesh, LEEP and Thermo-coagulator have acquired acceptability as a commonly used outpatient treatment procedure for CIN. Since the year 2010, “See and treat” strategy is offered for managing the colposcopy diagnosed high grade CIN cases.

So far the centres are providing opportunistic screening only without electronic data recording, Recently GOB is planning to initiate Population-based organized cervical cancer screening programme with referral from grass root level by CHCPs. The women of target group will have individual electronic registration and electronic data tracing for screening, evaluation and management of screen positive cases and a template for electronic data recording connected to DHIS2 is in the process of development. Public awareness campaigns, utilization of facilities, motivation of stakeholders, electronic data tracing and scaling up of facilities towards grass root level should have visible impact on spontaneous participation

Facility Readiness for Breast, Cervical and Oral Cancer Screening in India: Findings from the Fourth Round of District Level Household and Facility Survey (DLHS-4)

Capt. Mona Saraiya, CDC, USA, Preet K. Dhillon Mona Saraiya, S. Agrawal, A. Yadav, E. Van Dyne, B. Hallowell, V. Senkomago, S. Patel, CDC, USA

Background: India's National Programme for Cardiovascular Disease, Diabetes, Cancer and Stroke (NPCDCS) recommends screening of breast, cervical, and oral cancers for 30-64 year olds; public healthcare facility readiness to undertake this screening program has not been evaluated.

Methods: We examined healthcare facility resources for cancer screening in India's states and over 512 districts from DLHS-4 (cross-sectional cluster-randomized sample) data at 18,367 sub-centres (SC's), 8,540 primary health centres (PHC's) and 4,810 community health centres (CHC's), using India's Operational Framework for cancer screening (December 2016) against a benchmark “Toolkit: Improving Data for Decision Making in Global Cervical Cancer Programmes (ICDDP). DLHS indicators of staffing, infrastructure, equipment and supplies, infection prevention, medications and laboratory

supplies, and hospital data management represented the "Facility Readiness Assessment" component of the ICDDP toolkit. A summary score of these variables was created to indicate facility readiness.

Results: At SC's, PHC's and CHC's respectively, 85.7%, 74.0% and 90.3% of facilities possessed human resources to conduct population-level screening; 58.7%, 90.0% and 99.0% had non-continuous or continuous power supply; 32.8%, 77.3% and 96.6% had examination/labor tables; 27.0%, 69.0% and 89.3% had an autoclave/sterilizer; 51.9%, 82.5% and 72.3% with satisfactory (incinerator/pit) bio-waste disposal; and 95.3%, 91.9% and 92.3% with >1 indicator for a data management system. Summary scores varied widely across SC's (mean =9.5, SD = 3.1), were higher in pilot-testing districts of NPCDCS, and in moderate correlation with a state's level of socioeconomic development (correlation coefficient = 0.44).

Conclusions: Facility readiness varies for cancer screening across public healthcare resources, with specific training and supplies for cervical cancer screening not yet available/ready for assessment. A quantitative readiness tool may help state-level planning prepare for cancer screening as per operational guidelines under the NPCDCS Programme.

Background:

Global absence of standardized tools and guidance, technical expertise, and implementation support for countries that are seeking to collect and use high-quality data to monitor, evaluate, and improve screening and treatment programs prompted an initiative to improve and accelerate the availability of data by gathering information on data systems in select country contexts, and by developing global standards, tools, and guidance. Funding from the BMGF supported CDC Foundation and a consortium of partners that included CDC, WHO, and the George W. Bush Institute. Through CDC Foundation, Jhpiego led the development of Patient and Program Monitoring kit and the Facility Level Assessment for Cervical Cancer. The iterative process included inputs from a variety of experts and international agencies as well as results from field testing. The initiative resulted to a set of 5 final draft modules: Cervical Cancer Data and Data Systems Assessment, Population-based Survey Modules for Cervical Cancer, Cervical Cancer Prevention and Control Costing – Screening and Treatment Module, Patient & Program Monitoring and Facility-based Surveys for Cervical Cancer. WHO and CDC are reviewing these materials for final publications

The toolkit is expected to provide critical guidance for countries to monitor, evaluate, and improve screening and treatment programs as it is introduced and scaled to reach more eligible women.

Data use for improving screening outcomes with access to effective treatment

Enriquito Lu, Global Reproductive Heath Direcotor
JHPIEGO, USA

Session Goal:

Introduce Facility Level Assessment and Patient and Program Monitoring Components toolkit for improving performance and accountability of cervical cancer screening programs.

AOGIN - INDIA TEAM

The Bivalent and Quadrivalent Vaccine

Prof. Shakti Bhan Khanna
Indraprastha Apollo Hospitals, New Delhi

Cervical cancer still ranks as one of the leading female cancers. Prevention is still advocated by Gynaecological oncologists, since therapeutic modalities available are still not 100% effective in curing disease. In November 1991, a workshop convened by the International Agency for Research on Cancer (IARC) and the WHO officially concluded that, based on epidemiological and laboratory data, the association between Human Papilloma Virus (HPV) infection and cervical cancer is beyond reasonable doubt, and infection with human papilloma virus should be considered as cause to the development of cervical cancer. (1)

Human Papilloma Virus (HPV) infection is the most common sexually transmitted disease. The high risk HPV can cause cervical and anogenital cancers. HPV 16 and 18 cases approximately 70% of cervical cancers. HPV type 31,33,45,52 & 58 account for approx. 15-19% of cervical cancer. Low risk HPV types 6 and 11 can cause >90% condylometa acuminate also called anogenital warts.

HPV vaccination significantly reduces the incidence of anogenital cancer & genital warts. US food and Drug Administration (FDA) has licensed three HPV vaccines since 2006 i.e Gardasil, Gardasil 9 and Cervarix. Gardasil is a quadrivalent vaccine and cervarix is a bivalent vaccine. All three vaccines prevent infection with HPV type 16, 18, 9 and 10 Gardasil also prevents infection with HPV type 6 and 11 (Cause of 90% genital warts). Gardasil 9 prevent infection with the same 4 high risk HPV infection plus additional high risk HPV types 31,33,45,52 and 58.

HPV vaccine is recommended for routine vaccination of adolescents (including boys & girls) at age 11 or 12 upto 26 years but can be started at age 9 years.

HPV Vaccine

Three HPV vaccines have been licensed by the U.S Food and Drug Administration (FDA) since 2006. HPV vaccine is recommended for routine vaccination of adolescents (including girls and boys) at age 11 or 12 years, and can be started at age 9 years.

HPV vaccines	Bivalent/2vHPV (Cervarix)	Quadrivalent/4vHPV (Gardasil)	9-valent/9vHPV (Gardasil 9)
Manufacturer	GlaxoSmith Kline	Merck	Merck
Year Licensed	October 2009 - females	June 2006 - females; October 2009 - males	December 2014 - males and females
HPV types in vaccine	16 and 18	6, 11, 16, and 18	6, 11, 16, 18, 31, 33. 45. 52. and 58
Adjuvant in vaccine	AS04: 500 µg aluminum hydroxide 50 µg 3-*O*-desacyl-4'-monophosphoryl lipid A	AAHS: 225 µg amorphous aluminum hydroxyphosphate sulfate	AAHS: 500 µg amorphous aluminum hydroxyphosphate sulfate
Recommended for…	Females ages 11-12 (can start at age 9 years) Females ages 13 through 26 who were not adequately vaccinated previously	Females and males ages 11-12 (can start at age 9 years) Females ages 13 through 26 and males ages 13 through 21 who were not adequately vaccinated previously Males ages 22 through 26 with certain immunocompromising conditions; gay, bisexual, and other men who have sex with men (MSM); and transgender persons who were not adequately vaccinated previously	Females and males ages 11-12 (can start at age 9 years) Females ages 13 through 26 and males ages 13 through 21 who were not adequately vaccinated previously Males ages 22 through 26 with certain immunocompromising conditions; gay, bisexual, and other men who have sex with men (MSM); and transgender persons who were not adequately vaccinated previously
Contraindicated for…	People with anaphylaxis caused by latex	People with immediate hypersensitivity to yeast	People with immediate hypersensitivity to yeast

"Cancer Diagnostics Cytopathology – Transition from Post Genomic Era to Precision Medicine"

Dr Puneet Chandna, Mumbai

The objective of performing a test over a patient is to reduce uncertainty about the patient's diagnosis or prognosis and also to aid the clinician in making management decisions. In the clinical setting, precautionary care activities often can be incorporated in to the regular, constant or ongoing care of patients, such as when a doctor checks the blood pressure of a patient stressing upon the doctor with complain of a sore throat or orders pneumococcal vaccination in an older person after dealing with a skin rash. At other times, a special visit just for preventive care is scheduled; thus the terms annual physical, periodic check-up, or preventive health examination.

High sensitivity and specificity is the most essential criteria that applies to all including, all types of screening tests, whether they are history, physical examination, or laboratory tests. A good screening test must, therefore, have a high sensitivity so that it does not miss the few cases of disease present. It must also be sensitive early in the disease, when the subsequent course can still be altered. A screening test should also have a high specificity to reduce the number of people with false-positive results who require diagnostic evaluation.

Covering the two main types of cervical cancer: squamous cell carcinoma and adenocarcinoma, Screening can detect precursors and early-stage disease for both types. Conversely, Treatment of precursors and early-stage disease can prevent the development of invasive cervical cancer.

While cytologic screening for cervical cancer with Papanicolaou (Pap) test has never been evaluated in a randomized trial, multiple observational studies in various countries have shown reductions in cervical cancer incidence and mortality as screening is implemented. This has led to the adoption of screening programs in all developed and many developing nations worldwide. In addition to the Pap test, screening methods now include tests for high-risk strains of human papillomavirus (HPV), which are central to the pathogenesis of cervical cancer.

Visualisation, evaluation or sampling may become a challenge for some women patients in whom, the cervix is difficult to visualize on pelvic examination, it may be the case of the uterus sharply anteverted or retroverted. Yes and more, the vaginal fornices is some may be obliterated in women with vaginal atrophy due to menopause or other conditions (eg, prior pelvic radiation, vaginal graft-versus-host disease), and the cervix may not protrude in the usual fashion.

Various strategies can be used to increase screening rates. Active invitation to women to schedule an appointment for cervical cancer screening is an effective way to increase participation in a screening program.

Equipments and Indications for Colposcopy

Dr Geethanjali Amin, Mumbai

For effective Colposcopy as for any Endoscopic method, one must become familiar with the instrument and technique of the examination. Correct interpretation of Colposcopic findings is possible by three important things: 1. Good skill in colposcopy technique

2. Basic knowledge of the colposcopic theory and cervical pathology.

3. Availability of right instruments.

A Colposcope is a low power, stereoscopic, binocular microscope with a powerful variable intensity light source that illuminates the area being examined. A magnification range of 6x to 15x usually provides the requirement for a complete examination. Currently 3 types of colposcopes are available in the market.

1. Simple Optic colposcope with varied magnification.

2. Swivel arm colposcope which may have floor pedestrials or may have wall mounting or examination table mounting with or without camera and video monitor attachment.

3. Video colposcope with image management system.

Videocolposcope has increased patient satisfaction with preventive healthcare has increased the use by the Gynecologists on a day today practice since it has shortened the learning curve and user friendly.

The instruments needed for colposcopy are few, simple and not expensive but care should be taken not to compromise on any of them. To mention few important ones are: self retaining vaginal speculums, sponge holding forceps, good sharp biopsy forceps, Endocervical curettes, Endocervical speculums, long plane forceps, cotton balls, swab sticks and ribbon gauze. Saline, freshly prepared 5% Glacial acetic acid, Lugols iodine, Betadine solution and Monsels paint or silver nitrate crystals are the basic chemicals required for the procedure. Maintenance, disinfection of the instruments and disposal of the materials should be followed strictly.

Main role of colposcopy is to rule out invasive or diagnose early preclinical invasive cancer and secondly to grade the lesion, assist in directing a biopsy from the worst affected areas and finally to triage the case for the management of CIN.

The Indications for Colposcopy are the following:

1. All screen positive cases – cytology/ visual screen tests/ HPV test

2. Clinically suspicious looking cervix

3. Symptomatic though screen test negative

4. Post treatment surveillance

5. Medico legal cases- sexual abuse, rape victims

But for the beginners to get acquainted with the technique & colposcopy findings of normal, abnormal; it is better to practice colposcopy on all gynecological cases in their OPD practice, Pre operative cases routinely.

Impact and effectiveness of the quadrivalent human papillomavirusvaccine: a systematic review of ten years of real-world experience

Prof. Suzanne Garland, Melbourne, Suzanne M. Garland1, Susanne K. Kjaer2, Nubia Muñoz3, Stan L. Block4, Darron R. Brown5, Mark J. DiNubile6, Brianna R. Lindsay6, Barbara J. Kuter6, Gonzalo Perez6,7, Geraldine Dominiak-Felden8, Alfred J. Saah6, Rosybel Drury8, Rituparna Das6, and Christine Velicer6

Prophylactic HPV-vaccination programs constitute major public-health initiatives worldwide. We assessed the global effect of 4vHPV vaccination on HPV infection and disease. PubMed and Embase were systematically searched for peer-reviewed articles from January-2007 through February-2016 to identify observational studies reporting the impact or effectiveness of 4vHPV vaccination on infection, anogenital warts, and cervical cancer or precancerous lesions. Over the last decade, the impact of HPV-vaccination in real-world settings has become increasingly evident, especially among girls vaccinated before HPV exposure in countries with high vaccine uptake. Maximal reductions of ~90% for HPV 6/11/16/18 infection, ~90% for genital warts, ~45% for low-grade cytological cervical abnormalities, and ~85% for high-grade histologically-proven cervical abnormalities have been reported. The full public-health potential of HPV vaccination is not yet realized. HPV-related disease remains a significant source of morbidity and mortality in developing and developed nations, underscoring the need for HPV-vaccination programs with high population coverage.

AOGIN - India, Secretariat

Room No 2058

Rajeev Gandhi Cancer Institute & Research Centre,

Sector 5, Rohini, New Delhi 110085

Phone - 01147022027, 01147022058

Website - www.aoginindia.in

Key Recommendations of ASCO Resource-Stratified Clinical Practice Guideline (2016) for secondary prevention of Cervical cancer

Dr Nisha Singh, KGMU, Lucknow

Primary Screening

Human papillomavirus (HPV) DNA testing is recommended in all resource settings.

Visual inspection with acetic acid may be used in basic settings.

The recommended **age ranges and frequencies** in each setting are as follows:

Maximal: 25-65 years, every 5 years

Enhanced: 30-65 years, if two consecutive negative tests at 5-years intervals, then every 10 years

Limited: 30-49 years, every 10 years

Basic: 30-49 years, one to three times per lifetime

Exiting Screening

Maximal and enhanced: > 65 years with consistently negative results during past > 15 years

Limited and basic: < 49 years, resource-dependent; see specific recommendations age

TriageIn basic settings, visual assessment for treatment may be used after positive HPV DNA testing results.

If visual inspection with acetic acid was used as primary screening with abnormal results, women should receive treatment.

For other settings, HPV genotyping and/or cytology may be used.

After Triage

Women with negative triage results should receive follow-up in 12 months.

In basic settings, women should be treated if there are abnormal or positive triage results. THE BOTTOM LINE (

In limited settings, women with abnormal results from triage should receive colposcopy, if available, or visual assessment for treatment, if colposcopy is not available.

In maximal and enhanced settings, women with abnormal or positive results from triage should receive colposcopy.

Treatment of Women With Precursor Lesions

In basic settings, treatment options are cryotherapy or loop electrosurgical excision procedure (LEEP).

In other settings, LEEP (if high level of quality assurance) or ablation (if medical contraindication to LEEP) is recommended.

Twelve-month post-treatment follow-up is recommended for all settings.

Special Populations

Women who are HIV positive or immunosuppressed for other reasons should be screened with HPV as soon as diagnosed and screened twice as many times in a lifetime as the general population.

The management of abnormal screening results for women with HIV and positive results of triage is the same as in the general population

Women should be offered primary screening 6 weeks postpartum in basic settings and 6 months postpartum in other settings.

Screening may be discontinued in women who have received a total hysterectomy for benign causes with no history of cervical dysplasia or HPV. Women who have received a subtotal hysterectomy (with an intact cervix) should continue receiving routine screening.

Four-Tiered Resource Settings for Secondary Prevention

Basic Core resources or fundamental services absolutely necessary for any public health/ primary health care system to function; basic-level services typically are applied in a single clinical interaction; screening is feasible for highest need populations.

Limited - Second-tier resources or services that produce major improvements in outcomes, such as incidence and cost effectiveness, but that are attainable with limited financial means and modest infrastructure; limited-level services may involve single or multiple interactions; universal public health interventions are feasible for a greater percentage of the population than primary target group.

Enhanced - Third-tier resources or services that are optional but important; enhanced-level resources may produce further improvements in outcome but increase the number and quality of screening/treatment options and individual choice (perhaps ability to track patients and links to registries).

Maximal - May use high-resource setting guidelines; high-level/state-of-the art resources or services that may be used in some high-resource countries and/or may be recommended by high-resource setting guidelines that do not adapt to resource constraints; this should be considered lower priority than in the other settings on the basis of cost impracticality for limited-resource environment.