AOGIN India E newsletter

The quarterly newsletter of Asia Oceania research organization on Genital Infections and Neoplasia– India
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From the Editor's desk

Dear AOGIN India members,

Wish you a very

Happy and colorful Holi

It gives me immense pleasure to bring forth the second issue of our E newsletter. Brush up the WHO guidelines and welcome the nonavalent vaccine with a case study, journal scan and what we miss in a pap smear. Have a look at the AOGIN India March organized on World Cancer Day. Plan your travel to Lucknow and Vellore. Continue to send articles and suggestions for improvement.

With best wishes **Dr. Nisha**

Inside this issue:

Summary of "WHO Screen and Treat Strategy" Dr. Nisha Singh, KGMU, Lucknow

- The expert panel recommends against the use of CKC as a treatment in a screen and treat strategy. Therefore, all screen-and-treat strategies below involve treatment with cryotherapy, or LEEP when the patient is not eligible for cryotherapy.
- Use a strategy of **screen with an HPV test and treat**, over a strategy of screen with VIA and treat. In resource-constrained settings, where screening with an HPV test is not feasible, the panel suggests a strategy of screen with VIA and treat.
- Use a strategy of screen with an HPV test and treat, over a strategy of screen with cytology followed by colposcopy (with or without biopsy) and treat. However, in countries where an appropriate/high-quality screening strategy with cytology followed by colposcopy already exists, either an HPV test or cytology followed by colposcopy could be used.
- Use a strategy of screen with VIA and treat, over a strategy of screen with cytology followed by colposcopy (with or without biopsy) and treat. The recommendation for VIA over cytology followed by colposcopy can be applied in countries that are currently considering either programme or countries that currently have both programmes available.
- Use a strategy of screen with an HPV test and treat, over a strategy of screen with an HPV test followed by colposcopy (with or without biopsy) and treat.
- Use either a strategy of **screen with an HPV test followed by VIA and treat**, or a strategy of screen with an HPV test and treat.
- Use a strategy of screen with an HPV test followed by VIA and treat, over a strategy of **screen with VIA and treat**.
- Use a strategy of screen with an HPV test followed by VIA and treat, over a strategy of screen with **cytology followed by colposcopy (with or without biopsy) and treat.**
- Use a strategy of screen with an HPV test followed by VIA and treat, over a strategy of screen with an **HPV test followed by colposcopy (with or without biopsy) and treat.**

The five "screen and strategies" have been highlighted in sequence of recommendation preferred by WHO.

Adapted from WHO Guidelines 2013

New kid on the block: Gardasil 9

Dr. Shalini Rajaram, Delhi, President, AOGIN India

On December 10th, 2014 FDA approved the human papillomavirus vaccine by Merck, Gardasil 9, for protection against seven high risk HPV types namely 16,18, 31, 33, 45, 52, 58 and against HPV types 6,11 responsible for genital warts. It has the potential to prevent over 90% of cervical, vulvar, vaginal & anal cancers. Like the previous quadrivalent vaccine it is indicated in girls between 9 and 26 years of age for prevention of genital pre-cancers and cancer.

In males it is recommended from 9 through 15 years of age for prevention of anal intra-epithelial neoplasia, anal cancer and genital warts. However it must be remembered that in India any type of HPV vaccination is NOT licensed for use in males.

The vaccination is administered in three doses over 6 months and may provide a 'broader' protection. It has been studied in over 14,000 HPV naïve women aged 16-26 years and was found to be 97 percent effective. Injection site pain, swelling, redness and headaches are the commonly reported side effects.

Some unanswered questions – what should girls already vaccinated do? Repeat three courses? No answers from the company but it probably will be prudent to continue screening strategies. The previous vaccines probably offer adequate protection, as over 80% of HPV types in India are HPV 16 and 18. Will the new vaccine see a renewed interest in the prevention of cancers of the genital tract? What are the studies on prevention of oro-pharyngeal cancers caused by HPV? Is this vaccine really required – given that the uptake of previous vaccines is still poor even in developed countries? The bottom line is that vaccination coverage has to be improved come-what-may, hand-in- hand with screening, education, awareness, safe practices and of course political will! The population benefits seen with vaccination in Australia is phenomenal and must be taken as a model for cervical cancer prevention. In India, Tamil Nadu with its screening practices in place covering almost all districts is a prototypical model that other states must emulate and once this is in place GAVI may be approached for affordable vaccines.

Reference- Kirby T. FDA approves new upgraded Gardasil 9. Lancet Oncol 2015 Feb; 16(2): e56.

Journal scan : Dr. Bindiya Gupta UCMS & GTB Hospital, Delhi

Cancer Cytopathol. 2014 Mar;122(3):227-35.

Usefulness of p16/Ki67 immunostaining in the triage of women referred to colposcopy.

Ordi J, Sagasta A, Munmany M, Rodríguez-Carunchio L, Torné A, del Pino M.

BACKGROUND: This study compared the performance of p16/Ki67 dual-staining and human papillomavirus (HPV) testing in women referred to colposcopy and sought to determine the usefulness of a morphological evaluation of the double-stained cells.

METHODS: This prospective study included 1123 women (mean age, 35.8 ± 10.9 years) referred to colposcopy from October 2009 to November 2012 due to positive HPV testing or abnormal cytology results (atypical squamous cells of unknown significance, or worse abnormalities). Liquid-based cytology specimens (Preserv Cyt, Hologic) were used for HPV detection (Hybrid Capture 2 [HC2]; Qiagen) and p16/Ki67 dual-staining (CINtec Plus; Roche-mtm Laboratories). All women underwent histological study. After completion of the study, 18 patients were classified as having cervical cancer (CC), 378 had a high-grade squamous intraepithelial lesion (HSIL), 304 had a low-grade squamous intraepithelial lesion, and 423 were negative.

RESULTS: The sensitivity and specificity of p16/Ki67 dual-staining for HSIL/CC were 90.9% (95% confidence interval [CI] = 87.9-93.9) and 72.1 (95% CI = 68.7-75.4), respectively. For HC2, the figures were, respectively, 96.0% (95% CI = 93.9-98.0) and 41.4 (95% CI = 37.7-45.0). The values were high both in women < 30 and ≥ 30 years old (86.9% and 63.3% versus 92.3% and 77.8%, respectively). The addition of a morphological evaluation of the dual-stain-positive cells with establishment of HSIL features as the threshold for a positive reaction increased the specificity (93.5%) but decreased the sensitivity (84.1%).
CONCLUSIONS: Use of the molecular markers p16 and Ki67 has higher specificity than HC2 tests for HSIL or CC, which may support p16/Ki67 dual-staining use in the triage of patients referred for abnormal screening results. Morphological evaluation of p16/Ki67-positive cells may have some benefits in women younger than 30 years or with low-grade squamous intraepithelial lesion.

AOGIN India participation in 'Walk for Life - Stride against Cancer'- Dr Bindiya Gupta, UCMS

Members of AOGIN India from Delhi-NCR region participated under the AOGIN India banner in the Can Support eighth 'Walk for Life - Stride against Cancer' event on 8 February 2015, on Shanti Path, Chanakyapuri. Smt Sangeeta Jaitley, Wife of Finance Minister flagged off the walk and Manisha Koirala, Cancer Survivor, film actor and activist lead the Lap of Honour for Survivors. Students, prominent citizens and people from all sections of society walked shoulder to shoulder to express their solidarity with those living with cancer, and to mark World Cancer Day. The Lap of Honour organized for survivors was followed by the bikers, cyclists, runners and skaters then the walkers. There were a total of 20 schools, 27 colleges & 24 corporates participating in the Walk.

Pap smear examination: What we miss? Dr. Sharad Jain NSCB Medical College. Jabalpur

Any infection caused by bacteria, viruses, or protozoa in reproductive tract is RTI and if caused by unsafe sex is STI.. It is known to be a major cause for cervical cancer. There are chances of eight fold rise of HIV transmission in RTI &STI positive cases. Every day, more than 1 million people acquire STI worldwide. Women with STI may also have common symptoms like vaginal discharge, backache and pain during sexual intercourse. They are invariably subjected for Pap smear examination.

What we miss in a Pap smear examination is major challenging global task of RTI & STI. PAP smears are predominantly reported as negative or positive for malignant cells, smear pattern inflammatory or showing no specific pathology or changes. With such Pap smear reports the STI diagnosis is omitted or missed completely. Patient continues to suffer and spread STI. Considering globally such a high incidence of RTI & STI, there is an absolute need to evaluate any patient with clinico- cyto-pathological assessment for STI too. In clinically suspected cases of RTI & STI, who are economically compromised, both partners must be treated effectively during their first visit by NACO guided RTI, STI syndromic approach. Patient must be investigated along with Pap smear for HIV, HPV and HBV routinely. If test is found negative, vaccinate for HPV and HBV. RPR test (non specific) is available for syphilis. Gonorrhea can be diagnosed from discharge by Gram staining, Trichomoniasis can be diagnosed using Wet smear microscopy and Candidiasis by 10% KOH preparation.

Pap smears reporting is definitely important but imperfect method even for the diagnosis of cervical cancer and especially STI hence needs review and attention. Diagnosis and effective treatment for STI is sometimes missed with Pap smear reported as inflammatory pattern. It results into further spread of RTI/ STI and its related serious complications.

Case study favoring HPV E6/E7 mRNA detection Dr Dinesh Gupta, Ms Varsha Raina, New Delhi

Primary Presentation: A patient aged 41 yrs presented with c/o vaginal discharge intermittently for last 3 years. She was treated on the basis of syndromic approach with antibiotics, antifungal and anti-parasitic drug (Tinidazole). She had been married at 24 yrs with two normal deliveries and had regular periods. In May 2014, the patient found vaginal discharge irritating.

Primary Diagnosis: On examination, the cervix was healthy and no sign of vulvo-vaginal lesions. A mild dysplasia was suspected and sample was collected for concurrent HPV DNA, HPV E6/E7 mRNA (HPV OncoTect) and LBC .

The concurrent testing for LBC and HPV: A single sample was collected using cervi-brush in LiquiPrep preservative medium. The LBC was negative for malignancy but HPV DNA test showed a viral load of 5.4 (Positive) and HPV E6/E7 mRNA was borderline positive at 2.1% mRNA over-expression. The colposcopy did not reveal abnormal cervix and patient was asked to revisit after 3 months. A repeat LBC testing in Oct 2014 resulted in LSIL.

Colposcopic Findings: A colposcopy was able to identify acetowhite area between 4 to 5 O'clock positions with mosaic pattern spreading upwards at 3 O'clock position on the TZ towards cervical os. The underlying vascularity was observed as abnormal. The directed punch biopsy performed and micro-invasive squamous cell carcinoma was detected.

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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.

Upcoming Events