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From the Editors Desk

Dear friends

Wish you a very Happy New Year

I am delighted to bring out the fresh issue of our Newsletter. You will find glimpses of AOGIN India 2016 conference and workshop held at Patna; articles on HPV self-testing and SLNM in cervical cancer along with the journal scan.

Best wishes

Nisha Singh, Lucknow

What is inside

Office Bearers

AOGIN India 2016 Conference

Richa Singh, Patna

The 7th National conference of AOGIN India was organized from 14th to 16th October, 2016 at Patna. Dr. J.K Singh was the Organizing Chairman and Dr. Richa Chauhan was the Organizing Secretary. The theme of the conference was HPV Vaccination + Screening = Cervical Cancer Elimination. The conference had 8 international and 62 national faculties. 200 participants and 150 ASHAs and ANMs attended it.

Conference Day 1 started with free paper presentation followed by a session on the burden of HPV infection and associated gynecological cancer. Along with lectures and panel discussions on abnormal screening tests & pre-invasive disease, the keynote address was given by *Dr. R. Sankaranarayanan from France* on "*Global experiences in scaling up HPV vaccination and HPV testing and their impact". HPV Vaccination Fact Sheet of American Cancer Society and the print issue of AOGIN India newsletter were released.* There was a special session on *Cervical Cancer Control programs in India, Nepal, Bhutan, Bangladesh, Thailand and United Kingdom.* There was an interesting debate on the role of HPV vaccination in elimination of cervical cancer. *AOGIN India Oration on 'What does it take to be an expert colposcopist and how can I become one?' was delivered by Dr. Patrick Walker from England.* This was followed by the inaugural ceremony and cultural program with banquet.

On the second day, the free paper session and poster presentation was followed by a session on innovations in screening and vaccination, a video session on different surgical techniques used in the management of gynecological malignancies and a panel discussion on Genital warts and vulvar disease. The conference concluded with the valedictory function in which prizes were distributed by Dr. J.K Singh, and Dr. Shalini Rajaram, Dr. Divya Aggarwal, Delhi, Dr. Bindiya Gupta, Delhi and Dr. Sabuhi Qureshi, Lucknow won the 1st, 2nd and 3rd prizes in oral paper presentation. Dr. Mohit Jadli, Delhi, Dr. Himanshu Mishra, Lucknow and Dr. Basumita Chakraborti, Kolkata won the 1st, 2nd and 3rd prizes in poster presentation.

Workshop on "Cervical Cytology- Integration with HPV Detection"

14th October, 2016 Alok Chandra Bharti, Delhi

A Pre-conference workshop on "Cervical Cytology and its Integration with HPV Detection" was organized during 7th AOGIN-INDIA Conference. The workshop was co-ordinated by Dr. Prabhat Ranjan, Patna, Dr. Alok Chandra Bharti, Delhi and Dr. Priya Abraham, Vellore. The workshop was attended by 30 local pathologists and other conference delegates.

Dr. Ranjan gave the overview of cervical cytology with special emphasis on facts and artifacts of Pap smears and addressed commonly encountered problems during performance of a successful cytopathological evaluation. Dr. Bharti gave a succinct description of basic biology of HPV-induced carcinogenesis, HPV diagnostics and detailed how HPV detection can be integrated with cervical cytology at the point of sample collection. He informed the delegates about need of cytology beyond cervix like oral and anal cavity. Dr. Sandeep Mathur, Delhi presented a list of IHC Biomarker how they could be useful in the diagnosis of CIN lesions. The talks were followed by a lucid video demonstration of HPV Testing by Hybrid Capture II by Dr. Abraham. Subsequently, Dr. Puneet Chandna, Delhi, elaborated the importance of quality control and how to execute a robust quality control.

The workshop was vibrantly participated by PGs and Residents with a Quiz for PG students under the able guidance of the quiz master Dr. Pallavi Agarwal. The house was opened for questions, interactions and Panel discussion. The workshop ended with Quiz Results and Prize distribution. Three PG students were declared winners and awarded with certificates upon winning the Quiz.

Few more glimpses of the conference

Community screening workshop (14th October 2016)

Dr Latha Subramanium, Coimbatore

A community screening workshop was organized 14th October 2016. The objective was to assist in building capacity of community health workers (CHWs) in educating women and community members on relevant aspects of cervical cancer and breast cancer prevention. 145 ASHAs and ANMs belonging to the Government Health system from various districts of Bihar were the participants.

The workshop comprised of three sections – i) Theoretical sessions that were taken in local language (Hindi) so that CHWs could comprehend the contents better, ii) 4 Video demonstrations on methods of cervical sample collection, Cervical screening and breast examination, iii) Group activities to give opportunity to CHWs to learn by interacting with each other.

The participants were divided into 5 groups for Group activity on following topics:

Developing community awareness plans for cervical and breast cancer prevention'

Specific messages to be given to women on cervical & breast cancer?

Preparation for organizing screening in your locality

Developing community support for generating awareness about cervical & breast cancer?

The challenges that may arise in bringing women to the clinics for screening

The winning group leaders were given certificates by the coordinators.

Significance of HPV Self testing Dr Chanchal Rana, Lucknow

Cervical cancer is detectable and preventable through cervical screening for pre-cancerous lesions; however this is often not effective in most developing countries where adequate health infrastructure, human and financial resources are inadequate. Another reason is the embarrassment and concerns about discomfort that keep women away from attending smear tests. To avoid this problem, HPV self-sampling devices are now available in the market. With the help of these devices, women themselves can collect sample for HPV testing, in their own home, removing the need for them to go to the surgery or clinic for the test.

The lavage based device (e.g Delphi screener) produces a lavage-sample by rinsing the cervix and upper vagina with saline. Saline is released by pressing a plunger of the device and flows back into the device when the plunger is released.

However **the brush-based device (e.g Viba brush)** produces a dry sample by collecting cervical and upper vaginal endothelial cells when the brush is rotated in the upper vagina. The brush device is inserted in the vagina up to its wings, the brush is pushed out from the casing by pressing a plunger and rotated five times. These samples can be submitted in the laboratory where the cell sample is extracted from the brush by adding buffered saline. Finally the tests for various types of HPV can be performed in laboratory.

Petignat et al (2007) found a high level of concordance between self- and clinician-sampling for the detection of HR HPV DNA. A review by Peter J.F. Snijders et al (2013) suggested that HR HPV testing on self-samples appeared as sensitive for CIN2 as cytology or HR HPV detection on clinician-obtained cervical samples, though often less specific. This specificity reduction can be tackled by application of proper triage methods. The studies performed with brush- and lavage-based self-collection devices show an increased sensitivity for CIN2 compared to those performed with swab samples. However Arbyn et al (2015) in a meta-analysis included pooled data from 36 studies to compare the efficacy of HPV testing on self-collected samples to samples collected by clinicians. They found that although the sensitivity as well as specificity was lower in self collected samples, HPV self-sampling significantly improved the participation of women who did not routinely attend cervical cancer screening programs**.** Jeronimo et al (2014) conducted multicentric study including India and documented that it's sensitivity using cervical or vaginal self-collected samples was better than VIA or Papanicolaou test.

Hence, HPV testing on a self-sample can be suggested as an additional strategy to reach women not participating in the regular screening program, making it a potential alternative and ensuring that women who test positive by any method get timely follow-up and care.

Journal Scan — Dr Bindiya Gupta, New Delhi

Combined clinical and genetic testing algorithm for cervical cancer diagnosis.

Liou YL, Zhang TL, Yan T, Yeh CT, Kang YN, Cao L, Wu N, Chang CF, Wang HJ, Yen C, Chu TY, Zhang Y, Zhang Y, Zhou H. Clin Epigenetics. 2016 Jun 10;8:66. doi: 10.1186/s13148-016-0232-3. E Collection 2016.

BACKGROUND: Opportunistic screening in hospitals is widely used to effectively reduce the incidence rate of cervical cancer in China and other developing countries. This study was aimed to identify clinical risk factor algorithms that combine gynecologic examination and molecular testing (paired box gene 1 (PAX1) or zinc finger protein 582 (ZNF582) methylation or HPV16/18) results to improve diagnostic accuracy.

METHODS: The delta Cp of methylated PAX1 and ZNF582 was obtained via quantitative methylation-specific PCR in a training set (57 CIN2- and 43 cervical intraepithelial neoplasia ≥grade 3 (CIN3+) women), and the individual and combination gene sensitivities and specificities were determined. The detection accuracy of three algorithms combining gynecologic findings and genetic test results was then compared in a randomized case-control study comprising 449 women referred for colposcopic examination by gynecologists in the outpatient department of Xiangya Hospital between November 2011 and March 2013.

RESULTS: Significant association was observed between CIN3+ and methylated PAX1 or ZNF582 in combination with HPV16/18 (OR:15.52, 95 % CI:7.73-31.18). The sensitivities and specificities of methylated PAX1 or ZNF582 combined with HPV16/18 for CIN3+ women were 89.2 and 76.0 %, or 85.4 and 80.1 %, respectively. Of the three algorithms applied to cohort data and validated in the study, two indicated 100 % sensitivity in detecting cervical cancer and a low rate of referrals for colposcopy.

CONCLUSIONS: These algorithms might contribute to precise and objective cervical cancer diagnostics in the outpatient departments of hospitals in countries with high mortality and low screening rates or areas with uneven resource distribution.

Role of Sentinel Lymph node mapping (SLNM) in cervical cancer

Nisha Singh, Lucknow

Sentinel lymph node biopsy is currently the standard of care for certain malignancies, including melanoma and breast cancer.

The proposition that if SLN, being the first node that receives drainage from the primary tumor is negative for malignancy, the remaining regional lymph nodes would also be negative and a complete node dissection could be avoided has prompted a recent surge in the interest toward innovation, optimization, and validation of SLNM in early stage cervical cancer patients.

Currently, radical hysterectomy with pelvic lymphadenectomy is the standard of care for early stage cervical cancer. Pelvic node metastases are detected in 17 % of stage IB and 12–27 % of Stage IIA disease. Thus, we unnecessarily perform pelvic lymphadenectomy in about 70 % cases, which is avoidable with the use of SLNM. However, opponents of this technique have voiced concern that some nodal metastases may be missed if only the sentinel lymph nodes are removed.

Sensitivity of SLNM varies from 80-100%. Various studies have shown that concurrent use of radioisotope methods has the highest rate of SLN identification giving a sensitivity and NPV of 100%

Preoperative imaging of Sentinel Nodes can be done with Lymphoscintigraphy, a nuclear medicine scan where the lymph node basin is imaged after injection of radiocolloid in an attempt to identify the sentinel lymph nodes. Single photon emission computed tomography (SPECT) is another nuclear medicine imaging modality that utilizes gamma rays to provide three-dimensional imaging information. SPECT/CT appears to offer a significant improvement in sentinel node detection and anatomic localization as compared to lymphoscintigraphy.

Cyalume, methylene blue and isosulfan blue were the initial dyes investigated for sentinel lymph node biopsy (SLNB). Cyalume (a fluorescent dye) stains the lymphatics and surrounding tissue, generating a high background. Methylene blue, a water-soluble dye, demonstrated poor lymphatic uptake in initial studies but recent work shows that it can be a substitute for isosulfan blue and is less expensive. Diab Yaser (2016) found that ICG SN mapping has higher overall and bilateral detection rates. 71% of sentinel nodes are interiliac, 8% internal iliac, 5% external iliac, and 5% common iliac. Few investigators have found obturator nodes as the most common sentinel node. Most investigators have used 4cc of methylene blue injection around the tumor in 2, 4, 8 and 10 o'clock position or at 3, 6, 9 and 12 o'clock position.

Fig 1 : Sentinel Lymph Node mapping

Fig 2: Injection sites for the methylene blue dye

Diagnostic accuracy of sentinel lymph node mapping is increased by use of ultrastaging (the process of micro sectioning and immunohistochemical staining of the nodes in an attempt to detect metastasis), surgeon's experience and tumor size < 2 cm.

Cormier et al developed a sentinel lymph node mapping algorithm with the aim of detecting all lymph node metastases while limiting the number of lymphadenectomies. The algorithm suggested: 1) all mapped sentinel nodes are excised and ultrastaged, 2) all suspicious nodes are removed regardless of mapping, 3) if only unilateral mapping occurs, a contralateral lymphadenectomy is performed, and 4) all cases include parametrectomy en bloc with primary tumor resection. When this algorithm was evaluated in 122 women, 100% of positive lymph nodes were identified. Though these findings are encouraging, additional studies are needed to validate the algorithm.

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.

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Memberships invited. Please visit AOGIN India website

Forthcoming conferences

Masterclass in Gynaeoncology
7-8 January 2017
TMH, Mumbai

Annual RGCON
3rd-5th Feb 2016
New Delhi

Annual ISCCP Conference
New Delhi
3rd-5th March 2016