

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 friends,

Greetings

Hope this E-newsletter finds you in good health and high spirits. This issue includes an article on Gynocular by Dipanwita Banerjee, journal scan by Seema Singhal and AOGIN events by Bindiya Gupta. Namrata presents an article on role of VEGF. Enjoy reading and attend the upcoming conferences in Delhi and Agra.



Best wishes

Nisha Singh, Lucknow

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Potential role of VEGF in Cervical cancer

Dr Namrata, Dr Nisha Singh, Lucknow

Cervical cancer is the most common gynecological cancer in India. Prognosis of advanced or recurrent disease is extremely dismal with an overall survival of just over 12 months. Newer therapeutic interventions were therefore required to be searched for. Advances in understanding of mechanisms of tumor growth and spread and effects of human papilloma virus (HPV) infection identified angiogenesis as a rational target for therapeutic intervention in cervical cancer. The HPV oncoproteins E5, E6, and E7 are the proven primary viral factors responsible for initiation and progression of cervical cancer. E6 and E7 play key roles in up regulating angiogenesis through the VEGF pathway through their effects on p53 degradation.

Angiogenesis appears as a critical step in carcinogenesis and tumor progression. Although numerous proangiogenic factors have been described in literature, the VEGF family of ligands (VEGF A to D); the placental growth factor (PLGF) and their associated receptor tyrosine kinases (VEGFR 1, 2 and 3) are the most important regulators of angiogenesis. VEGF-A binds to VEGFR-1 and VEGFR-2; the stimulation of endothelial cell mitogenesis and vascular permeability is mediated by its interaction with VEGFR-2. PLGF and VEGF-B selectively bind to VEGFR-1 and stimulate vessel growth and maturation and recruit proangiogenic bone marrow-derived progenitors. VEGF-C enhances cervical cancer invasiveness via up regulation of Gal-3 protein through NF- κ B pathway, which may shed light on potential therapeutic strategies for cervical cancer therapy.

Anti-angiogenic agents showed promising activity in early phase clinical trials culminating in a randomized phase III study of the humanized monoclonal antibody to vascular endothelial growth factor (VEGF), **Bevacizumab**, in combination with chemotherapy. Gynecologic Oncology Group protocol 240, has met its primary endpoint demonstrating a significant improvement in survival. Bevacizumab emerged as the first targeted agent to be granted regulatory approval by the United States Food and Drug Administration for use alongside chemotherapy in adults with persistent, recurrent or metastatic carcinoma of the cervix.

Exploration of novel anti-angiogenic agents targeting parallel angiogenesis related pathways are being undertaken and considered in women with cervical cancer. Single agent, orally administered, multi-TKIs, Pazopanib (VEGFR 1, 2, and 3; PDGFR- α and β ; and c-KIT inhibitor) and Sunitinib (VEGFR 1, 2 and 3; PDGFR, c-KIT, and FLT3 inhibitor) have been investigated. Recently, the CIRCCa trial evaluated Cediranib for primary metastatic or relapsed cervical cancer. However, as CIRCCa closed prematurely owing to the cessation of commercial production of Cediranib, Brivanib, another drug which targets VEGFR 2 and FGFR-1, is currently being evaluated in a phase II study (NCT01267253) conducted by the GOG.

The current scenario suggests that there are breakthrough advances in newer drugs and therapies. Yet, the key point to betterment of health remains prevention and early detection of the disease for which we are committed.

Journal Scan**Dr Seema Singhal, AIIMS New Delhi****Results of delayed triage by HPV testing and cytology in the Norwegian Cervical Cancer Screening Programme****Haldorsen T , Skare GB , Ursine G, Tone bjorge. Acta Oncologica, 2015; 54: 200-209**

Objectives : High-risk human papilloma virus (hr HPV) testing was added to the cytology triage of women with equivocal screening smears in the Norwegian programme for cervical cancer screening in 2005. In this population-based observational survey before and after study the effect of changing the screening algorithm were studied.

Materials and methods: In periods before and after the change 75, 852 and 66, 616 women, respectively, were eligible for triage, i.e. they had smear results of unsatisfactory, atypical squamous cells of undetermined significance (ASC-US), or low-grade squamous intraepithelial lesion (LSIL) at routine screening. The triage was delayed as supplementary testing started six months after the initial screening. The groups were compared with respect to results of triage and later three-year cumulative incidence of cervical intraepithelial neoplasia grade 2 or worse (CIN2 +).

Results: Before and after the change in the screening algorithm, 5.2% (3964/75 852) and 8.1% (5417/66 616) of women, respectively, were referred to colposcopy. Among women referred to colposcopy cumulative incidence of CIN2 + (positive predictive value of referral) increased from 42.0% [95% confidence interval (CI): 40.3 - 43.7%] in the period with cytology only to 48.0% (95% CI 46.6 - 49.4%) after the start of HPV testing. For women recalled to ordinary screening the three-year cumulative incidence decreased from 2.7% (95% CI 2.5- 2.9%) to 1.0% (95% CI 0.9 - 1.2%) during the same period. Among women with LSIL at routine screening and HPV testing in triage, 52.5% (1976/3766) were HPV positive.

Conclusion: The new algorithm with HPV testing implemented in 2005 resulted in an increased rate of referral to colposcopy, but in a better risk stratification with respect to precancerous disease

Gynocular - A compact, magnifying device to triage VIA and HPV positive women in cervical cancer screening program

Dipanwita Banerjee Ranajit Mandal, Partha Basu

The recent guidelines from World Health Organization (WHO) recommended the 'screen and treat' approach for the women positive on either VIA or HPV test without colposcopic or histological verification. Treatment without histological verification on the basis of colposcopy diagnosis (see and treat) is quite often practiced even in developed countries. Colposcopy is gradually losing ground as a diagnostic tool in the low resource settings due to several limitations. The equipment is bulky, technically complex, expensive, needs electrical supply and quite cumbersome to be set up in primary health settings. We do require a compact, user friendly, technically less demanding device with comparable precision with standard colposcope but can be used limited resource set up.

The Gynocular™ (Gynius AB, Stockholm, Sweden) is a compact monocular device with three step magnifications (5X, 8X and 12X), LED illumination, green filter and rechargeable battery. The major advantage of the device is its portability, completely battery driven and also comes with a tripod stand which makes it feasible to use in remote settings where carrying a heavy weight standard colposcope is not possible. A separate application named Gynocular T2D (Triage to diagnosis) is available, where the pictures of the gynocular findings can be taken by any smart phone using the application even without any requirement of internet access. The pictures along with patient details can be uploaded by cloud computing. The only disadvantage of the device is its monocular vision and completely manual focusing.

Experience in a community set up: The cross-sectional community based study conducted between April 2014 to March 2015 by the Department of Gynecologic Oncology, Chittaranjan National Cancer Institute (CNCI) in the rural districts of West Bengal. Total 6921 women aged between 30 to 60 years were screened by VIA and HPV DNA test. Total 684 screen positive women were examined by Gynocular™ and subsequently cervical punch biopsy was taken. The Gynocular findings were interpreted using both IFCPC 2011 colposcopy terminology and Swede score. The sensitivity and specificity of Gynocular™ in detecting IFCPC Grade 2 findings were 93% and 96% respectively. The ROC curve plot estimated the sensitivity at varying swede score cutoff values showed an optimum combination of high sensitivity and specificity could be achieved at the swede score of 5.

Conclusion: Gynocular™ with its T2D application has the potential to be used as a triaging device for VIA or HPV positive women in resource limited set up due to its portability, logistic advantage of being battery operated and lower cost. It definitely gives an edge over naked eye examination in picking up the precancerous lesions more precisely followed by taking guided biopsy and serving definitive treatment.

Pictures on page 6

AOGIN India Events-Picture gallery**Bindiya Gupta, UCMS, New Delhi****Gynocular training course**

Gynocular training course was organised under the aegis of AOGIN India at UCMS and GTB Hospital, Delhi on 9th November 2015 by Dr Shalini Rajaram and her team. There were 10 participants from various places in North India including Lucknow, Gurgaon, Delhi and Madhya Pradesh. The course coordinator Mr Vikas from Hyderabad gave hands-on training in using gynoculars, supporting software and uploading of data on the gynocular database. Overall the workshop was successful and an enriching experience.

**Cervical Cancer Awareness Program for ANMs**

The second camp of the AOGIN initiative of training of ASHA and ANM's for cervical cancer awareness was organised by Department of Obstetrics and Gynaecology, Babu Jagjivan Ram Memorial Hospital, Jahangirpuri, on 23rd October, 2015. The program was organized by Dr. Sumita Mehta, Secretary ISCCP, and Dr Anshul Grover was held in two batches of 100 ANMs of North district each. Various lectures were taken to sensitize the ANMs regarding cervical cancer and its screening. A quiz was held at the end of the lecture session and prizes were given. The program went off successfully. The participants benefited immensely from the interactive academic session and were very receptive about the information imparted to them. Participation certificates were handed over to all delegates.



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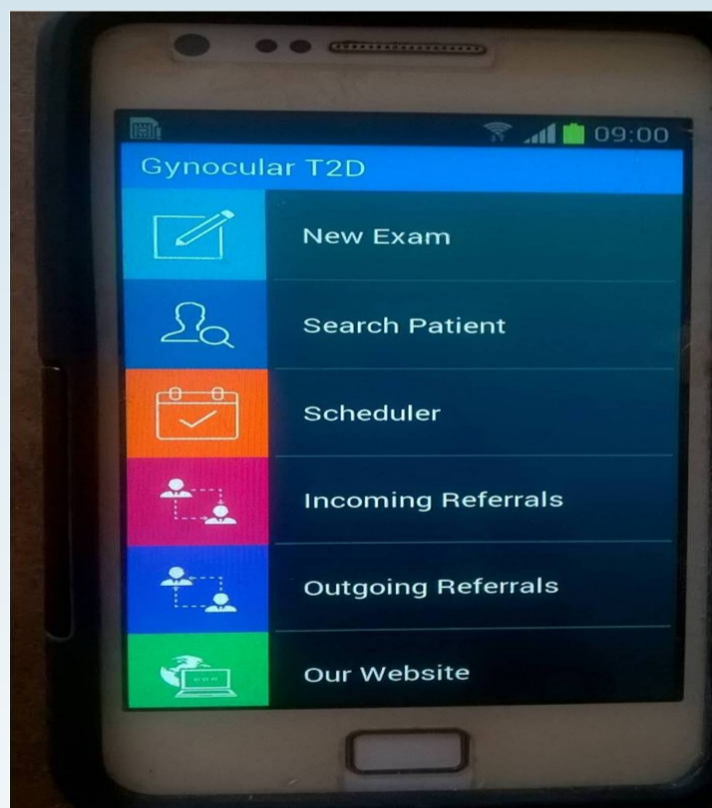
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Vision Statement

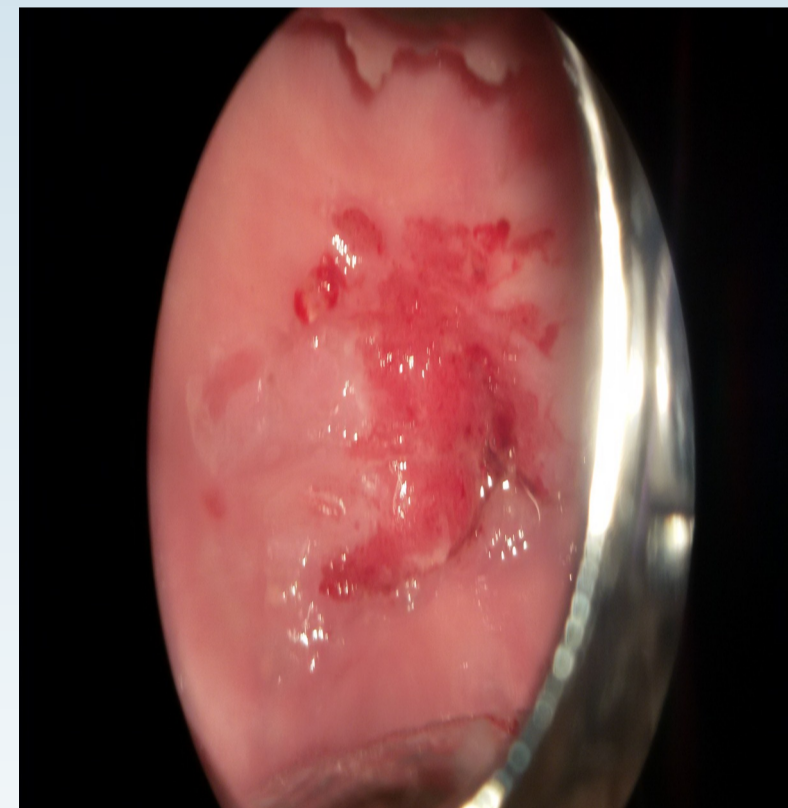
AOGIN India's vision is to reduce the burden of diseases caused by reproductive tract infections, especially Human Papillomavirus (HPV), in India. Furthermore, AOGIN India's **mission** is to work with governments, non-governmental organizations, learned societies, health care workers and the lay public, 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.



Gynocular device



T2D Application



Acetic acid application

Upcoming Events

AICOG

13-17th Jan 2016

Agra

International Conference

CONFIRMED SPEAKERS
Dr. Richard Barakat, President IGCS, MSRCC, USA
Prof. Neville Hacker, Australia
Dr. Subir Nag, Santa Clara, USA
Dr. Sean Dowdy, Mayo Clinic, USA

RGCON
From Controversy to Consensus
Gynae Oncology
5th - 7th February, 2016
India Habitat Centre, New Delhi

WHO SHOULD ATTEND?
Gynaecologists, Gynae Oncologists, Medical Oncologists, Surgical Oncologists, Radiation Oncologists, General Surgeons, Pathologists, Nuclear Medicine Specialists and Post Graduates in Concerned Specialities

HIGHLIGHTS OF THE CONFERENCE
Live Workshops, Panel Discussions, Masterclass - Case Capsules, Debates in Clinical Practice, Quiz & Abstracts

Last Date for Abstract Submission : January 10th 2016
Registration Charges : For Consultants ₹ Rs 2500/-, Onspot Registration - Rs 4000/-, For Post Graduates & Trainees - Rs 1000/-

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