THE QUARTERELY E-NEWSLETTER

AOGIN INDIA

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Asia Oceania research organization on Genital Infections and Neoplasia-India

From the Editors Desk

Dear Friends,

Warm Greetings,

I am extremely delighted to bring out the print version of our Newsletter at the 7th AOGIN India Conference at Patna.

You will find glimpses of AOGIN 2016 at Singapore and some great work by AOGIN members. Read about screening in HIV positive women, treatment with Cold coagulation and the journal scan.

Best wishes

Prof. Nisha Singh
Lucknow

What is inside

Office Bearers

AOGIN 2016 Singapore

Prof. Nisha Singh, Lucknow

Organized by AOGIN in collaboration with Society of cervical pathology & colposcopy of Singapore and O & G society of Singapore. The theme was- **New Frontiers in cervical cancer prevention**

Workshops - 12th August 2016

The workshops and Indonesia country Forum were conducted on 12th August 2016. The conveners of Cytology/HPV testing workshop were A Cheng, SC Lian and Philip IP. The conveners of the Video Pelvic surgery workshop were EH Tay and RM Noor. The Indonesia Country Forum was chaired by Y M Hidayat and F Kusuma.

Conference Day 1- 13th August 2016

The conference started with ASCCP session chaired by WL Wong and IS Ismail. The parallel IARC session was chaired by LK Tan and J Tan. Dr Sankarnarayan gave an encouraging talk on WHO and IARC's position on control of HPV related diseases and cervical cancers. Session on Future of Cervical cancer prevention was chaired by R Konno and S Ruey.

The **opening ceremony** was grand and had a true Indian flavor expressing gratitude to AOGIN President Dr Neerja Bhatla. The ceremony was chaired by herself and EH Tay. The program opened with a dance performance by 9-15 year old children. Dr Neerja Bhatla gave the presidential address on "Control of HPV related diseases and cervical cancer in Asia-Oceania in the last 15 years' and There was a perspective lecture by P Castle on "Cervical cancer prevention beyond Medical innovation".

Conference Day-2 14th August 2016

The India country forum was chaired by Dr Neerja Bhatla and Dr. Shalini Rajaram. The speakers were Dr Smita Joshi, Dr Rupinder Sekhon and Dr Sabhyata Gupta. Progress in implementation of cervical cancer program was presented by Dr Shikha for UP, Dr Sharmila for Maharashtra and Dr Shalini for New Delhi.

In addition, there was a breakfast symposium, colposcopy refresher course and a session on cervical cancer treatment. Phillipines country forum was chaired by J T P Luna and speakers were V Dy Echo, C Z Castro, B Toral and V Germar.

Congratulations to the Indian Awardees

Out of 60 research papers, 16 were from India and 8 selected for oral presentation. **Dr Vijaya Srinivas** was awarded for her paper "Performance of Gynocular T2D in Cervical cancer screening with visual inspection with acetic acid in assessing precancerous lesions in Mysore". **Dr Ritu Agarwal** was awarded for her paper, "Differential expression of Toll like receptor Transcriptome in HPV infected Cervix and Sq cell carcinoma".The conference concluded with AOGIN General assembly and closing ceremony. The next AOGIN conference will be held at Sydney in October 2018.

Cervical Cancer screening in HIV positive women

Prof. Nisha Singh, Lucknow

Cervical cancer in HIV positive women is a special case both due to the high morbidity and increased surgical risk to the operating team. B Clarke (2002) suggested that the more aggressive behavior of cervical neoplasms in HIV positive women is because of an accelerated progression via the microsatellite instability pathway, whereas the pathogenesis in HIV negative women involved loss of heterozygosity. Peter Memiahet al (2012) showed the role of HIV induced immunosuppression in the pathogenesis of cervical abnormalities and precancerous cervical lesions. A recent study at our institute showed a significantly ($P < 0.001$) high incidence of cervical lesions in HIV positive women (15.9.%) compared to HIV negative women (1.5%). CD4 counts below 500/cmm and HIV infection for more than 2 years were associated with an increased incidence of cervical neoplasia ($P<0.00I$). It is important to understand the need for regular and more frequent screening of these women, which is not a routine policy at most ART centers. WHO (2013) Screen-and-treat strategies for HIV-positive or unknown HIV status in areas with high endemic HIV infection are as follows:

Screening Method	Treatment indication	Post Rx Follow up	If Test is negative, Rescreen with
HPV	HPV positive	1 yr	HPV-Within 3 yr
HPV f/b VIA	HPV and VIA positive	1 yr	HPV-Within 3 yr; VIA - after 1yr
VIA	VIA positive	1 yr	VIA -Within 3 yr
HPV f/b colposcopy	HPV and colposcopy positive	1 yr	HPV/Colposcopy- Within 3 yr
Cytology f/b colposcopy	Cytology ≥ ASCUS and Colposcopy positive	1yr	Cytology- 3yr

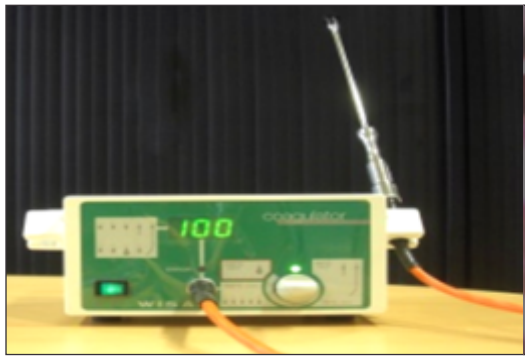
Choice of strategy- If existing screening program is VIA based and resources permit HPV test, Use HPV or HPV followed by VIA. If there is no existing program, and resources permit HPV test, Use HPV or HPV followed by VIA. If resources do not permit HPV, use VIA alone. If existing screening program is cytology followed by colposcopy (meeting quality indicators) and resources permit HPV test, Use HPV or cytology followed by colposcopy.

Thermocoagulation for the treatment of CIN

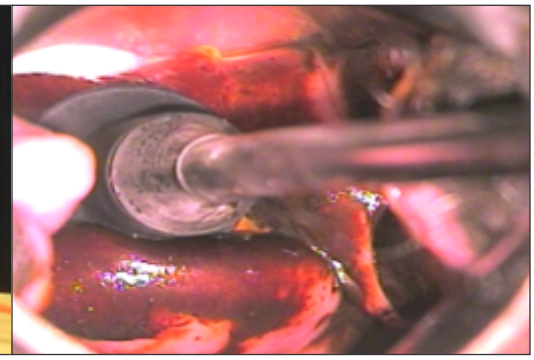
Dr. Smita Joshi, Pune

Cervical cancer is preceded by cervical abnormalities called cervical intraepithelial neoplasia (CIN). The objective of cervical cancer screening is early detection and treatment of CIN so that cervical cancer can be prevented. CIN 2 and 3 lesions are considered as high-grade lesions and they must be treated. CIN can be treated by ablative or excisional treatment modalities. A meta-analysis of the effectiveness and safety of different treatments options for CIN which included 29 trials showed that there is no obvious superior technique for treating CIN in terms of treatment failures or operative morbidity. The most commonly used ablative treatment method is Cryotherapy. 'Thermo coagulation' or 'Cold coagulation' is also an ablative treatment procedure for the treatment of CIN and has been in use in Europe and South America for the past 35 years. However, recently it has drawn significant attention from the scientific as well as medical community.

The Cold Coagulator



Treatment by Cold coagulator



A meta-analysis that evaluated the efficacy of cold coagulation for the treatment of CIN has reported cure rate of 96% [95% confidence interval (CI) 92-99%] and 95% (92-98%) for the treatment of CIN1 and CIN2-3 disease respectively. 'Cold coagulation' is in fact a misnomer and it is actually heat coagulation in which a heated probe is used for the ablation of the epithelium. The procedure can be performed as an outpatient procedure and does not require any local anesthesia as it is well tolerated by almost all women. Treatment with thermo coagulation can be used in a 'screen and treat program' or 'screen, see and treat program' or when there is a biopsy confirmed CIN.

Advantages over cryotherapy- The treatment time with Thermocoagulation is shorter, multiple overlapping applications may be given, there is less patient discomfort and the instrument is handy. It does not require filling/re-filling of gas that is required for cryotherapy however it requires electrical supply that may not be readily available in remote, rural settings. Efforts are on going to develop a low-cost, battery operated thermocoagulation unit.

Indications - Treatment with cold coagulation may be offered when there is type 1 transformation zone (TZ) fully visible squamo-columnar (SCJ) in which one can trace the SCJ in its entirety, lesion involves <75% TZ, lesion is entirely located on the ectocervix, there is no endocervical canal or vaginal involvement, no suspicion of invasive cancer, no history of pregnancy and the woman should be at least 3 months post-partum and should not be menstruating. We can perform cervical biopsy safely before any ablative treatment.

Technique- After a written informed consent, the woman should be asked to empty her bladder and lie down in a modified lithotomy position. Cervix should be exposed with a self-retaining bivalve speculum (Cusco or Grave) and acetic acid should be applied to delineate the lesion. Lugol's iodine may be applied if available, which further helps in delineating the lesion. A biopsy may be obtained whenever possible. The probe should be heated to 120 degree centigrade and allowed to remain at this temperature for a minute and then the temperature should be lowered to about 105 degree centigrade. The first application should cover the external os and the recommended treatment time is 45 seconds (when the probe is at 100 to 105 degree centigrade). In order to cover the entire lesion, multiple (4 to 5) overlapping applications of 45 seconds each may be given.

Side effects – It is generally well tolerated but some women may complain of mild pain, vaso-vagal attack, abdominal cramps, bleeding, vaginal burns (due to careless application) or PID.

Advice on discharge and Follow-up- Women should be instructed to abstain or use barriers for 6 weeks. There could be watery/blood stained discharge for 4 to 6 weeks. Antibiotics are prescribed if there is evidence of cervical or vaginal discharge prior to treatment. Follow-up visit is advised after 6 weeks to 3 months to assess the healing and then after one year. The risk of persistence or recurrence remains high for treated CIN for 8-10 years. HPV test can be done at 12 months as a 'test of cure'. If the test is positive, the woman should be investigated and treated if required.

3D: Spreading awareness to eradicate cervical cancer an initiative

Dr Deeksha Pandey, Manipal

3D – Dreams, Desires, Destiny is a group of volunteers who aim to create a sexually, psychologically and emotionally healthy generation of Indian adults, by spreading awareness and diverting energy towards positivity and creativity. The organization aims to spread awareness on the eradication of cervical cancer. 3D team, works with vigorous passion to educate and eradicate cervical cancer.

The research directorate of Manipal and the Rotary club support the 3D venture. It was one of the 80 projects that were started on the 80th birthday of Dr. RamdasPai, Chancellor of Manipal University. 3D has conducted, to date, 10 workshops in most of the colleges of Manipal University. The aim of these workshops is to create awareness about cervical cancer and sexually transmitted diseases with an emphasis on their consequences.

The youth are made aware about related issues such as HPV, HIV, and vaginal infections. The participants are made aware of safe sexual practices, and other techniques that help to prevent STDs. There are two kinds of workshops conducted, on the basis of age group i.e., 18-30 and 30-60. To make sessions more interactive, the participants are formed into groups, and asked to perform a skit/ role play based on the disease that their group has received.

These workshops conclude within the stipulated time of three hours. We also tailor fun games to facilitate learning.

The 3D team has around 88 volunteers from various walks of life, which forms the strength of 3D. Together, 3D wishes to fulfill the aim of seeing an informed and knowledgeable India and one day hope to see a cervical cancer free India.

Camp organized by AOGIN India members

Dr Madhu Gupta Ghaziabad

Beautiful Tomorrow Trust, in association with AOGIN India, organized a Colposcopy camp at Community Health Centre, Muradnagar, on 6th June 2016. Chief Medical Officer, Ghaziabad inaugurated the camp.

Doctors of the Trust had screened 300 women between the ages of 30 to 50 years by VIA, in cervical cancer screening camps organized in the area over the past 2 and a half months. Out of these females, 20 VIA +ve cases were shortlisted for Colposcopy. During the above colposcopy camp, out of the 20 coploscopies, 7 colposcope guided biopsies were done. Biopsy reports showed chronic cervicitis. These patients have been listed for Cryotherapy, which will be done in very near future.

Journal Scan

Dr Bindiya Gupta, New Delhi

Parents' Support for School-Entry Requirements for Human Papillomavirus Vaccination: A National Study.

Calo WA, Gilkey MB, Shah PD, Moss JL, Brewer NT.Cancer Epidemiol Biomarkers Prev. 2016 Sep; 25(9):1317-25. doi: 10.1158/1055-9965.EPI-15-1159. Epub 2016 Aug 19.

BACKGROUND: The number of states proposing school-entry requirements for human papillomavirus (HPV) vaccination has increased over the last decade. However, data are currently limited regarding parents' support of such laws. We sought to obtain the first national estimates of parents' support of HPV vaccination school-entry requirements.

METHODS: A national sample of 1,501 parents of 11- to 17-year-old children completed a web-based survey between November 2014 and January 2015. Analyses used multivariable logistic regression to assess correlates of support for school-entry requirements for HPV vaccination.

RESULTS: Overall, 21% of parents agreed that laws requiring HPV vaccination for school attendance "are a good idea," and 54% disagreed. If school-entry requirements included opt-out provisions, agreement increased to 57%, and only 21% disagreed. Parents more often agreed with requirements without opt-out provisions if they were Hispanic [OR = 1.53; 95% confidence interval (CI), 1.05-2.22], believed HPV vaccine was as or more important than other adolescent vaccines (OR = 2.76; 95% CI, 1.98-3.83), or believed HPV vaccine was effective for preventing cervical cancer (OR = 2.55; 95% CI, 1.93-3.37). Parents less often agreed if they resided in Midwest states or believed that HPV vaccine was being pushed to make money for drug companies (both $P < 0.05$).

CONCLUSION: Opt-out provisions almost tripled parents' support for HPV vaccine school-entry requirements. Our findings suggest that race/ethnicity, attitudes about HPV vaccine, and region of residence may influence support for requirements without opt-out provisions.

IMPACT: Opt-out provisions greatly increase parent support of school-entry requirements for HPV vaccination but may make them ineffective.

Letter to Editor

"Condylomaacuminata to carcinoma cervix-cytology and beyond it" published in June 2016

Comments made by Dr Dinesh Gupta:

1. "Cervical lesions are the one where cytology plays as significant a role". Proven to be otherwise. Even in the organized population settings, it is differed to 3 to 5 yrs for its poor predictability and authenticity. It still remains highly variable interpretation. A time for clinicians to appreciate it.
2. "Majority of cases are induced by HPV infection. HPV 6 and 11 are the most common cause". Strange to find types 6 & 11 linked to CIN, despite two decades of awareness for India..
3. "Degradation of human p53 and pRb proteins causing acceleration of the cell cycle and aberrant S-phase induction". causes deregulation of cell cycle through repeated chromosomal abnormalities and blocking apoptosis.
4. "The combination of ProExC and p16 had the highest sensitivity whereas the combination of p16 and Ki67 had the highest specificity." Why does one need a high sensitivity over and above hc2 proven through many many studies? ProExC is a better marker of cell cycle regulation and get overexpressed in early stage DNA replication. These stains prove worth while in tandem use in enhancing specificity for CIN2+ but they can not distinguish between LSIL or HSIL. So even their specificity is seen very moderate in some recent studies.

Response by Author, Dr Ridhi Jaiswal:

1. Cervical lesions are the one amongst all gynaecological diseases where cytology plays a significant role. Though newer diagnostic and screening methods are available, it is still a commonly used test worldwide.
2. HPV types are classified by their association with cancer. Non-oncogenic, or low-risk HPV types, such as HPV 6 or 11, can cause (1) benign or low-grade abnormalities of cervical cells, (2) anogenital warts, and (3) a disease of the respiratory tract called recurrent respiratory papillomatosis (RRP). Oncogenic, or high-risk HPV types, including types 16 and 18, can cause intraepithelial neoplasia of the anogenital region, including cervical, vulvar, vaginal, penile, and anal cancers as well as some oropharyngeal cancers.[Weinstock H, Berman S, Cates W, Jr. Sexually transmitted diseases among American youth: incidence and prevalence estimates, 2000. Perspect Sex Reprod Health 2004;36:6-10]. I apologize for the deletion of some part of the statement in the article.
3. Regarding the role of p53 and Rb genes, the following articles may be referred to:Dyson N et al. The HPV virus 16 E7 oncoprotein is able to bind to the Rb gene product. Science. 1989; 243:934-37. Wemens BA et al. 1990; 248:76-79.The induction and maintenance of HPV-induced neoplastic cervical epithelium requires incorporation of the viral genome into the host cell DNA resulting in the loss of the inhibitory effect of E2, an early gene product on E6 and E7 oncogenes, which in turn promotes the degradation of human p53 and pRb proteins causing acceleration of the cell cycle and aberrant S-phase induction. In this process, the anti-apoptotic property of these genes also plays role.
4. As I found in the existing literature, these stains do differentiate between LSIL and HSIL, however differentiating a condyloma from LSIL is difficult. In any case, a test that is both sensitive and specific, is always desirable. Study by Badr et al, already quoted in the article.

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 stall or visit the website

Forthcoming conferences

IGCS Biennial conference
29-31st October 2016,
Lisbon, Portugal

AGOI CME
13th November 2016
Lucknow, UP, India

AGOICON 2016
2nd-4th December 2016
Gurgaon, India