

AOGIN INDIA

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From the Editors Desk

Dear friends

Season's Greetings

Very happy to bring out this spring issue of our E Newsletter. It includes an insight into Sampoorna clinics running in UP, thoughts on HIV and HPV, cervical cancer camp in Midnapore and the regular journal scan. Enjoy reading and sharing.

Best wishes

Nisha Singh, Lucknow



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What's inside

Page1	From the Editor
Page 2	Awareness and screening program
Page 3	Journal Scan
Page 4-5	UP Govt Initiative- Sampoorna
Page 6-7	Is HPV or HIV first
Page 8	Forthcoming events

Cervical And Breast Cancer Awareness And Screening Program Dr Dipanwita Banerjee, Dr Ranajit Mandal

The Department of Gynaecologic Oncology at Chittaranjan National Cancer Institute, Kolkata is currently overseeing a population based Cervical Cancer Screening Program (CCSP), utilizing visual inspection with acetic acid (VIA). As per the World Health Organization's (WHO) recommendation, the project is based on "Screen and Treat" strategy for cervical cancer prevention.

A breast and cervical cancer awareness and screening camp was organized under the aegis of AOGIN India at Pratapdighi, East Midnapore on 6th January, 2017. A team of three health workers, one coordinator, Dr Ranajit Mandal and Dr Partha Basu visited the camp.

The program started with an orientation session and an awareness talk on breast cancer and cervical cancer, explaining the importance of cancer screenings, self breast examinations and detecting the disease in its pre-invasive and early stage.



Approximately 15 ANMs, ASHA workers & the women willing to participate in the program along with the village Headman were present during the awareness session. A total of 60 women were recruited after taking informed consent and underwent cervical cancer screening with visual inspection on acetic acid. The women who were positive on VIA were immediately taken up for colposcopy and biopsy at the same time. After randomization, the screen positive women

were treated by one of the ablative modalities - Cryotherapy or Thermo coagulator.

Apart from 4 cases of VIA positive women who received treatment, 6 HPV DNA test positive women from a previous camp attended this event and received treatment. In addition to the cervical cancer screening, general health check up was also done and tablets of iron, folic acid and albendazole were distributed among the women attending the camp. At the end of a hectic day, the team was happy to have concluded the program successfully. Such small initiatives driven especially for the women residing in the rural areas, will create a larger impact in the overall belief to serve the community better.



Discovery of new methylation markers to improve screening for cervical intraepithelial neoplasia grade 2/3.

Boers A, Wang R, van Leeuwen RW, Klip HG, de Bock GH, Hollema H, van Criekinge W, de Meyer T, Denil S, van der Zee AG, Schuurin E, Wisman GB

Clin Epigenetics. 2016 Mar 9; 8: 29. doi: 10.1186/s13148-016-0196-3.

BACKGROUND: Assessment of DNA promoter methylation markers in cervical scrapings for the detection of cervical intraepithelial neoplasia (CIN) and cervical cancer is feasible, but finding methylation markers with both high sensitivity as well as high specificity remains a challenge. In this study, we aimed to identify new methylation markers for the detection of high-grade CIN (CIN2/3 or worse, CIN2+) by using innovative genome-wide methylation analysis (MethylCap-seq). We focused on diagnostic performance of methylation markers with high sensitivity and high specificity considering any methylation level as positive.

RESULTS: Methyl Cap-seq of normal cervixes and CIN2/3 revealed 176 differentially methylated regions (DMRs) comprising 164 genes. After verification and validation of the 15 best discriminating genes with methylation-specific PCR (MSP), 9 genes showed significant differential methylation in an independent cohort of normal cervixes versus CIN2/3 lesions ($p < 0.05$). For further diagnostic evaluation, these 9 markers were tested with quantitative MSP (QMSP) in cervical scrapings from 2 cohorts: (1) cervical carcinoma versus healthy controls and (2) patients referred from population-based screening with an abnormal Pap smear in whom also HPV status was determined. Methylation levels of 8/9 genes were significantly higher in carcinoma compared to normal scrapings. For all 8 genes, methylation levels increased with the severity of the underlying histological lesion in scrapings from patients referred with an abnormal Pap smear. In addition, the diagnostic performance was investigated, using these 8 new genes and 4 genes (previously identified by our group: C13ORF18, JAM3, EPB41L3, and TERT). In a triage setting (after a positive Pap smear), sensitivity for CIN2+ of the best combination of genes (C13ORF18/JAM3/ANKRD18CP) (74 %) was comparable to hrHPV testing (79 %), while specificity was significantly higher (76 % versus 42 %, $p \leq 0.05$). In addition, in hrHPV-positive scrapings, sensitivity and specificity for CIN2+ of this best-performing combination was comparable to the population referred with abnormal Pap smear.

CONCLUSIONS: We identified new CIN2/3-specific methylation markers using genome-wide DNA methylation analysis. The diagnostic performance of our new methylation panel shows higher specificity, which should result in prevention of unnecessary colposcopies for women referred with abnormal cytology. In addition, these newly found markers might be applied as a triage test in hrHPV-positive women from population-based screening. The next step before implementation in primary screening programs will be validation in population-based cohorts.

UTTAR PRADESH GOVERNMENT INITIATIVE- "SAMPOORNA": A COMPREHENSIVE WOMEN HEALTH CARE SCREENING & TREATMENT PROGRAM

Shikha Srivastava, Lucknow



Sensitive to the healthcare needs of women, the Government of Uttar Pradesh launched the Sampoorna Project in the year 2015 as a unique initiative dedicated to screening and treating women for all major non-communicable diseases in the state. The project "Sampoorna" launched under the umbrella of National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Disease and Stroke (NPCDCS) brings forth the preventive approach towards the non-communicable diseases (NCDs) in women.

The project not only aims to screen for diseases but also makes women aware about life style modifications and screening approaches which are important for prevention of NCDs including cervical and breast cancers.

The project was initially launched in five districts to pilot the proof of concept and document learning for scale up. It has now been expanded to additional 23 districts in the state. Under this Project, "Sampoorna clinics" have been established at district women hospitals and selected community health centres for screening and management of diabetes, hypertension, Cardio Vascular Diseases, cervical Cancer and breast cancer amongst women aged 30-60 years.





The clinics are being operated by a team of trained female health care providers, to serve women with utmost privacy and belongingness. Training sites have been established at Medical Colleges for capacity building of different health care professionals on screening techniques and management of the diseases covered under the project. To roll out the program, a Memorandum of Understanding was signed between National Health Mission (NHM), State Innovations in Family Planning Services Agency (SIFPSA) and Population Services International, India (PSI), wherein NHM supported with the funds, SIFPSA lead implementation and PSI provided technical support.



MOTHER- DAUGHTER approach is adopted to strengthen service delivery and public reach out. As per this approach, mother coming for comprehensive health checkup can bring her daughter aged 9 to 14 years for HPV vaccination on fix days at vaccination points in District Women Hospital.

Recently on 25th Feb 2017 HPV Bivalent vaccine was launched under “Sampoorna” project.

Bivalent vaccine is available in pre-filled liquid form and no reconstitution is required.. Two doses of vaccine are to be given to the girls aged 9-14 years, at least 6-12 months apart. The interval between two doses should not be less than 6 months and not more than 12-15 months. The vaccine is to be given intramuscularly in the outer side of deltoid (left upper arm). Mothers of adolescent girls will be mobilized by Sampoorna Clinic staff, Front Line workers – ANMS, ASHA and Paramedics. UP government vision is to end cervical cancer from the state by providing both HPV vaccine and screening services to eligible girls and women of the state.



Is HPV or HIV first**Dr Dinesh Gupta, New Delhi,**

A question over the decades that haunts evolutionary virologists the most, is whether infection with HIV precedes the HPV, or vice versa. Both of these viruses are sexually transmitted, are highly communicable and affecting larger populations, both the viruses cause deadly diseases (regardless of a syndromic phase of HIV, which would invariably lead to AIDS- a life threatening disease), one does not identify gender bias whereas the other affects mostly women!

HPV favors HIV acquisition and later takes a major burden of genital neoplasia or invasive cancer owing to sustained immune suppression. Though HPV is a much widely prevalent virus, HIV is not. Till date total number of strains of HPV known to cause cervical or lower anogenital cancers have gone up to 19, with nearly 70-75% burden being shared by two types (16 and 18) in the Indian context, HIV-1 is the more predominant over the only other strain HIV-2. Most men and women would acquire HPV sometimes during their life but only a miniscule of them would get HIV, at least among the population exhibiting co-infection.

Therefore, one tends to think, which one of these two, would occur first in an individual! And if this is universally true, whether it is population dependent, habitual or lifestyle dependent!! More progressively, will this factor have any encumbrance or benefit in selecting a therapy for either of these viral diseases. Current evidences however show that the incidence of cervical and lower genital cancers have not decreased due to antiretroviral therapies among co-infected population. Immune suppressed individuals due to factors such as HIV infection or organ recipient are known to be at an increased risk for lower anogenital cancers. Does this analogy holds true for temporary immune suppression during pregnancy or prolonged use of oral contraceptives many women experience in their life time, for instance, or does it make them more vulnerable to acquire new HPV infections even amongst the monogamous relationships? This is difficult to prove. In fact, this may not be analogous to compromised immunity due to HIV infections or organ transplant. How does the bodily immunity run differently in some individuals, also needs to be clearly understood! How long the deficient immunity must prevail to allow progression of high-grade pre-cancers to invasive state, needs to be understood.

Fringe studies so far prove that a sustained immunosuppression is not a determinant for progression to invasive cancer. The temporary innate immune response results in to adaptive immunity after the HPV infection, which inhibits various molecular signaling pathways such as interferon or other cytokine expression pathways. Does this make women more susceptible for HIV? This too looks unlikely due to the fact that mode of transmission is different for these two viruses; one is blood-born and the other one is not. Though both are potent STIs, decreased immunity does play a common role towards disease progression.

Comparing the Propensity of Co-infections:

HIV affects approximately 1.25 million people annually in the US but HPV only contributes to 1100 new cases of cervical cancer, thanks to an organized screening program since past four decades. The scenario in India is just opposite. India is estimated to have around 86,000 new HIV infections in 2015 and nearly 131,000 new cases of cervical cancer, owing to the non-existence of an organized cancer screening! Though some of the states in India have just begun screening by VIA/VILI as a primary modality due to affordability factor, it is a matter of concern how effective such one-time screening intervention may be if not covering a larger section of the target population, followed up by call-recall in every three to five year intervals.

Is our public health system geared up to meet this challenge of a change! Though the efficacy of VIA/VILI has been proven to be equal or better than cytology in India, it is very critical that a quality control measures must be strictly followed across the board among the health workers and clinicians engaged in to this program at the community level. No cancer screening program can ever be called successful unless a diseased population is treated appropriately and in the case of cervical cancer it may be more pertinent to monitor the treated population for immune status for at least ten years. It is only then that we can ensure no other opportunistic infections such as HIV or more rampant tuberculosis turning them more susceptible as they age. The incidences of HAART failure or development of drug resistant strains of mycobacterium (MDR and XDR) are increasingly becoming important in the Indian context.

Moving Forward:

Though only recently identified, HPV must be prevalent in humans since ages. HIV, however seems to be a modern virus, mutated over several thousand generations in wild animals prior to lately inflicting humans. Yet both of these viruses have not been able to evolve genetically; HPV being a double stranded DNA virus and HIV a single strand RNA virus.

Whichever virus comes first, studies so far show that the progression of carcinogenesis among HIV women is very aggressive with poor response to therapy as well. The recurrence rate among women with in situ carcinoma or even frank cervical cancer is also far more rapid among HIV positive women after anti-retroviral treatment. So is the case with the mortality outcome among these two cohorts starting with the anti-retroviral therapy as a baseline. It is therefore very important that the early initiation of appropriate medical care and intervention is planned for HIV-positive women.

Indian healthcare however does not provide adequate importance to preventive care and management. The emphasis on disease diagnosis is low, notwithstanding an organized screening. Many a times, diseases are predicted and treated. It seems we are in far too rush to conclude and treat. So is our population at large, largely guided by the clinical opinion placed before them. The dreaded infections like HPV or HIV need thorough investigations at the genetic and epigenetic level to understand and treat patients accordingly with a better outcome. The benefits of preventive healthcare for women can be many, as more recently CDC study finds, “women who were never or rarely screened for cervical cancer had a higher prevalence of ever reporting 1 of 7 chronic conditions including CHD, COPD, arthritis, depression, kidney disease, or diabetes”. May Indians draw some inspiration out of this study!

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

International FOGSI Gyne Oncology Conference

11-13th August

Bhubaneswar

Email- fogsionco2017@gmail.com

AOGIN India 2017

8-10th September 2017

Lucknow

Email- editor.newsletter@aoginindia.in