Volume 6 | Issue 2 | May-August 2016 | Price Rs. 5.00

# Newsletter

ISCCP

Member International Federation of Cervical Pathology and Colposopy

# Newsletter of Indian Society of Colposcopy & Cervical Pathology (Reg.)

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## From the Editor's Pen

Dear Friends,

Welcome back to the latest edition of the Indian Society for Colposcopy and Cervical Pathology (ISCCP) newsletter. Our aim is to bring the recent updates and trends in the field of cancer cervix and colposcopy from places in India. We thank you for sharing experiences, brainstorming newer techniques and bringing to the table interesting topics for debate in each issue.

This issue has focused on few informative articles which are off the beaten track. Managing cervical pre-invasive disease in pregnancy is a difficult situation for any trained colposcopist and only evidence based guidelines can come to our rescue. These have been touched on in this issue and beautifully highlighted in a review by Dr Ankita & Dr Sumita. Colposcopy in private practice is a different ball game from the government sector and the nuances, pros and cons have been outlined along with supportive data from his centre by one of our authors, Dr Parwate. The latest in the field of HPV vaccines, the nonavalent vaccine has been discussed in detail by Dr Sujata. What's new in the form of research and practice has been complied in journal scan by the editorial team. We hope you enjoy this issue as much as we enjoy bringing it out.

We are happy to announce that the next annual conference of ISCCP is slated to be held at Delhi in the second week of March 2017. It is a fantastic opportunity for members and those who are interested in this niche field to meet the experts and deliberate on the latest developments in the field. Registrations will open soon. Hoping to see you in large numbers to make this event a huge success!

Dr Pakhee Aggarwal
Dr Roopa Hariprasad
Editorial Team
ISCCP

## Announcement

All life members of ISCCP are requested to pay Rs 2,000/-to retain their membership of International Federation of Cervical Pathology and Colposopy for 5 years. Cheques in favor ISCCP may be sent to:

**ISCCP**
G-367 (Ground Floor)
Preet Vihar, New Delhi 110092, India.



**Forthcoming Conference**

**ISCCP**
**Annual Conference**
at New Delhi

Block the dates
11th-12th March, 2017

# CIN in pregnancy: treat, wait or interrupt?

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Cancers of the female genital tract are the most common malignancies encountered during pregnancy. Among them, cervical cancer is the most frequent accounting for almost 70% of genital tract neoplasia. Cervical neoplasia (including carcinoma in situ and invasive carcinoma) is estimated to complicate 1.5-12/100,000 pregnancies[1]. Overall 3% cases of cervical cancer are newly diagnosed in pregnant women per year. *The authors strongly opine that all unscreened pregnant patients undergo cervical cancer screening at the time of their prenatal visit, as pregnancy can represent a unique opportunity to approach otherwise unscreened women.*

Currently, the precise effect of pregnancy on HPV infection course is not fully known. In literature, the "paraphysiological" mmunological tolerance that characterizes pregnancy may promote the infection or may reduce the immune system effectiveness in clearing infection itself. Consistent with these immunological aspects, some authors found an increased incidence of high risk HPV subtypes in pregnant patients when compared with non- pregnant women[2]. Younger mothers and those with high parity had higher rates of HPV infection. One large population based cohort study found that CIN or cervical cancer affected women tended to be of lower socioeconomic status than healthy ones.

Regarding the natural history of CIN in pregnancy, most of cases remain stable or regress. Progression to invasive carcinoma is extremely rare, occurring in less than 0.4% cases. In fact, CIN 1 or LSIL has been associated with acceptably low rates of progression. Spontaneous regression occurs in 48-70% of HSIL (CIN2 & CIN 3) lesions.

The American Society for Colposcopy and Cervical Pathology (ASCCP) 2013 guidelines state that all pregnant patients should undergo Papanicolaou test (PAP smear) screening at the time of their initial prenatal exam. Overall, the Papanicolaou test, both with conventional and liquid based cytology, has sensitivity of 70% to 80% for detecting high-grade cervical neoplasia in pregnancy. According to cytological and pathological analysis, pregnancy related hormonal changes can promote modification of squamous and glandular epithelial cells, including hyperplasia and endocervical atypia, inflammation and endocervical gland hyperplasia and hypersecretory appearance (Arias-Stella reaction) giving false positive results. The follow up of a normal Papanicolaou test, obtained in antepartum period is same as in non-pregnant population[3].

## Diagnosis of CIN in Pregnancy

The diagnosis and management of premalignant cervical lesions in pregnancy still represents a strong challenge for clinicians and patients. Clinical options for CIN are not well defined worldwide and are mainly based on data taken from non-pregnant women, expert opinions, and retrospective case studies in pregnancy. The vascular cervix associated with gravid condition and the risk of premature pregnancy loss mandates deviation from existing consensus guidelines in screening for cervical cancer in pregnancy and treating associated CIN.

### *Colposcopic evaluation*

Colposcopic evaluation for CIN is easier to perform in pregnancy as squamocolumnar junction (SCJ) and transformation zone (TZ) are better exposed due to physiological eversion of columnar pattern. On the other hand increased pelvic congestion of cervix, vaginal wall protrusion and thick mucus formation limits its evaluation. As per recommendations if colposcopic evaluation in early gestation is unsatisfactory, it should be repeated in second trimester when complete eversion of SCJ and TZ are more likely detected.

### *Cervical Biopsy*

Biopsies are only indicated when colposcopic evaluation of cervical lesion is suspicious of invasive carcinoma or biopsy results could impact management options. Although, due to risks of uncontrollable bleeding from hyperemic and congested pregnant cervix prevent physicians to perform biopsies.

### *Endocervical curettage*

ECC is strongly contraindicated in pregnant patients as there are more chances of preterm deliveries and low birth weight babies.

## Management of CIN in Pregnancy

ASCCP 2013 Recommendations[4]:

1) Pregnant women older than 30 years with ASC-US on PAP smear to be managed as non-pregnant woman i.e HPV testing with exception that colposcopy may

be deferred until 6 weeks postpartum.

2) Patients who are hr-HPV negative can be followed with PAP test at 6 weeks postpartum.
3) Pregnant patients with Atypical Glandular cells(AGC) and Adenocarcinoma in situ (AIS) on PAP smear are referred for colposcopy (recommended) but endocervical curettage is unacceptable.
4) Patients with CIN-1: Postpartum follow-up is recommended without any treatment. For such women, additional colposcopic and cytological examination during pregnancy is unacceptable. Colposcopy is preferred for non-adolescent pregnant women with LSIL, but deferring this procedure until 6 weeks postpartum is also an option.
5) Patients with histological diagnosis of CIN2 and CIN 3: These women may undergo additional colposcopic and cytologic examinations at intervals no more frequent than every 12 weeks during pregnancy. Repeat biopsy during pregnancy is advisable only if the appearance of lesion worsens or cytology suggests invasive carcinoma. Pregnant women with HSIL who are not diagnosed with CIN2 or CIN3 should undergo reevaluation with cytology and colposcopy no sooner than 6 weeks postpartum.

## Treatment Modalities

Treatment during pregnancy such as ablation or excision is not indicated. Diagnostic excisional procedure such as conization is only indicated in case the suspicion for micro-invasive disease is high, colposcopy is unsatisfactory, or cytology and colposcopy do not correlate. The risks for obstetric complications such as haemorrhage, cervical incompetence and fetal loss need to be discussed with patient.

### *Large loop excision of TZ*

It is an excisional procedure having both diagnostic and therapeutic advantage. In this procedure abnormal area from transformation zone is excised in one sweep from side to side. Several authors have reported that depth of cone removed predicts degree of prematurity, particularly if it exceeds 10-12mm. Despite reported obstetric complications like preterm delivery, premature rupture of membranes, LLETZ can be performed with reasonable degree of maternal safety. Most recent ASCCP consensus guidelines states that it is only indicated in patients in whom invasive disease is strongly suspected at colposcopy or confirmed with biopsy.

### *Cold knife conization*

In this procedure, a cone shaped area of cervix with base at ectocervix and apex at the level of the internal os is removed using knife. This procedure is associated with heavy vaginal bleeding in 5-15% of pregnant patients. Furthermore, rate of spontaneous abortion is as high as 25%. Approximately 50% of patients will have recurrent CIN following an antepartum conization presumably secondary to smaller than usual excisions. For all these considerations, and according to present indications for treatment of CIN in pregnancy, cold knife conization is no longer indicated or performed.

### *Coin biopsy*

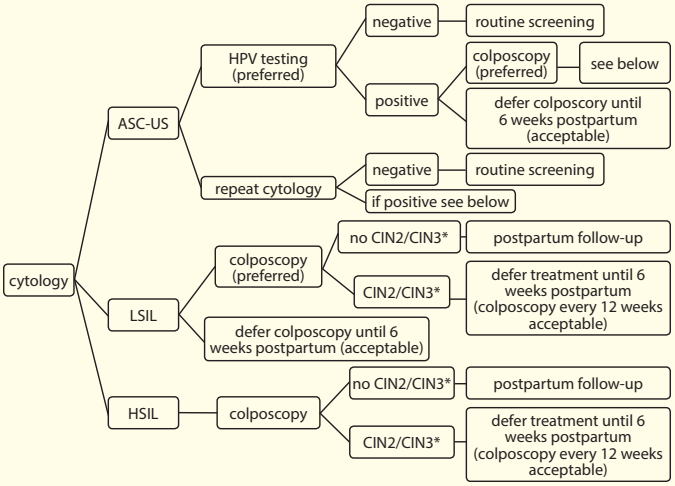
Because pregnancy causes a relative eversion of squamo-columnar junction, high sampling of endocervix may not be necessary. Some have advocated the excision of a coin shaped specimen instead of a cone shape in which the specimen is wedged out in shape of a pie, such shallow excision will cause less disruption to endocervical canal and may decrease both bleeding and preterm labor. The purpose of such excision is to diagnose invasion and not to treat intraepithelial neoplasia[5].

## Complications

High-risk HPV cervical infection detected in pregnancy is a risk factor for preterm birth. Some studies reported that women with cervical cancer, but not with CIN are at higher risk of delivering prematurely. They did not find any correlation between CIN or cervical cancer and increased risk of IUGR, PPROM and intrauterine death. In this regard, the only evidence based obstetrical complication correlated with presence and treatment of CIN in pregnancy is represented by significant increase in preterm deliveries in treated patients.

## Mode of Delivery

With regard to CIN no study has demonstrated relationship between mode of delivery and rate of regression. Patients with intraepithelial disease should have a mode of delivery that is based only on obstetric factors as well as maternal factors not related to CIN.



In conclusion, the role of colposcopy in pregnancy is to rule out invasive cancer so that treatment of CIN can be deferred until after delivery. Biopsy is to be avoided during pregnancy unless there is suspicion of high grade dysplasia or invasive cancer; here too endocervical curettage is contraindicated. A postpartum assessment is essential in all women with CIN during pregnancy.

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# Value of colposcopy as referral, in absence of national cervical cancer screening programme


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## Introduction

With a staggering 1 woman dying due to cancer cervix in India in every 7 minutes, it is high time that subject of cervical cancer pre cursors should be made a mandatory training protocol (every post graduate examination should have atleast 8 marks reserved for screening, and cervical cancer pre cursors) before obtaining a post graduate degree. It is time that every gynaecologist in the country should have basic training for understanding screening, performing atleast diagnostic colposcopy, otherwise there is no point crying why India contributes such a bulk to the global cervical cancer burden!

## Objective

As a private practitioner of colposcopy, the author studied all the referrals that were made for colposcopy in view of: 1) abnormal Pap smear report or 2) suspicious cervix with normal Pap smear, from July 2015-July 2016. In absence of any guidelines/ systems for cervical cancer prevention, a dedicated, trained colposcopist plays an invaluable role in correctly picking up pre-cancerous lesions and micro invasive cancers.

## Methods

A total of 138 patients between the age group of 28 to 49 years, including 6 post-menopausal women were referred with a) abnormal smear (94 patients), b) unhealthy cervix with normal smear (44 patients) during the study period. They all underwent colposcopy, at which 83 patients (4 with normal smears and 79 with abnormal smears) had pre-cancerous lesions detected and underwent biopsy. The remainder 55 patients (40 with normal smears and 15 with abnormal smears) had normal colposcopy findings and did not undergo biopsy. These 55 patients were asked to undergo liquid based cytology (LBC) after 3 months which were all normal and they were referred back to the primary gynaecologist to follow up at 3 yearly intervals. All referral smears were reported in the Bethesda 2015[1] system at the author's request.

The study was carried out in a private hospital in the western suburbs of Mumbai, with all facilities and infrastructure for colposcopy and oncology services. HPV based testing were not done as per ASCCP guidelines, as all patients were referred for colposcopy by primary doctors and currently there are uniform guidelines for HPV testing in the country. Patient population was middle income and higher middle income group as per Indian standards.

Out of the 138 patients, 121 patients had Pap done by conventional method and 17 had LBC. Colposcopy was done using IFCPC nomenclature of 2011[2]. All colposcopically suggestive lesions of CIN as per Swede score[2] underwent loop biopsy. The average size of biopsy specimen was 0.5 X 0.7cm. The final biopsy findings were compared with the CIN grading on colposcopy.

CIN 1 was treated by cryotherapy, while CIN2/3 underwent LLETZ. Post treatment the patient with cryotherapy underwent LBC at 6 months repeated again after 6 months, LLETZ patients underwent LBC with colposcopy at 6 months and LBC at 6 months. Colposcopy findings were more accurate for higher lesions CIN2+, as compared to CIN 1 lesions[3].

## Results

Of 138 patients, 44 patients had unhealthy cervix with normal smear, 30 patients had ASCUS, 42 patients had LSIL, 14 patients had HSIL, 4 patients each had ASC-H and AGS. Colposcopy findings in all these patients are given in Table 1.

**Table 1 :** Colposcopy findings in all patients (n=138)

| Smear report | Patients | Normal | CIN 1 | CIN 2 | CIN 3 |
|---|---|---|---|---|---|
| NILM | 44 | 39 | 4 | 1 | - |
| ASCUS | 30 | 10 | 16 | 3 | 1 |
| LSIL | 42 | 6 | 26 | 8 | 2 |
| HSIL | 14 | - | - | 6 | 8 |
| ASC-H | 4 | - | - | 2 | 2 |
| AGS | 4 | - | - | 1 | 3 |

Above table also included smear reports done by LBC. The colposcopy findings in those patients who had LBC in place of conventional Pap smear is given in Table 2.

**Table 2:** Colpscopy findings in patients with Pap done by LBC (n=17)

| LBC Report | Patients | Normal | CIN 1 | CIN 2 | CIN 3 | IA1/2 |
|---|---|---|---|---|---|---|
| NILM | 2 | 2 | - | - | - | - |
| ASCUS | 3 | - | 2 | 1 | - | - |
| LSIL | 5 | - | 4 | 1 | - | - |
| HSIL | 3 | - | - | - | 3 | - |
| ASC-H | 2 | - | - | - | 2 | - |
| AGS | 2 | - | - | 1 | 1 | - |

From tables 1 and 2, colposcopy findings were more accurate for high grade lesions. All LBC smears corroborated very well with colposcopy findings as seen from Table 2.

For the 55 patients where colposcopy findings were normal, a biopsy was not done. Colposcopy and biopsy co-relation for 83 patients with abnormal colposcopy is given in Table 3.

**Table 3:** Correlation of biopsy with colposcopy findings (n=83)

| Colpo findings | Patients | Normal | CIN 1 | CIN 2 | CIN 3 | IA1/2 |
|---|---|---|---|---|---|---|
| CIN-1 | 46 | 17 | 29 | - | - | - |
| CIN-2 | 21 | - | 3 | 16 | 2 | - |
| CIN-3 | 16 | - | - | 2 | 12 | 2 |

Of the 83 biopsies done for colposcopically suspect pre-cancerous lesions, 17 patients had normal biopsy reports and 66 patients had pre-cancerous lesions on biopsy, which gives 79.5% accuracy for colposcopy. For high grade (CIN2,3) disease, of the 37 patients who had suspected high grade lesions on colposcopy, 32 patients had confirmed biopsy finding which gives 86.4% accuracy of colposcopy for high grade lesions. Also two patients with micro invasive carcinoma were diagnosed (both had IA1 disease). Out of 46 patients with colposcopically suspected low grade lesions (CIN1), 29 patients had biopsy proven CIN1, which gives accuracy of 63.04% for low grade lesions[4]. However, 17 patients underwent biopsy for colposcopically suspect lesions but the final histopathology was normal so 12.1 % patients underwent unnecessary biopsies[4].

## Conclusions

A dedicated and trained colposcopist is a must for regions where there is absence of national cervical cancer screening programme .Gynaecologists trained in this speciality, with better understanding of pre-cancerous and cancerous lesions are able to achieve reasonable degree of accuracy of 86.4% for high grade lesions[5]. This is what is required for a country like India which contributes to the major global cervical cancer burden. LBC smears should be utilised in a screening programme because of their simplicity and clarity as there are false negatives with conventional Pap smear. HPV tests were not done in this study as there was no surety of follow ups, vague interpretation of HPV based tests and with such a huge burden of disease it was thought better by the author to view the cervix with colposcope. Thus, take a colposcopic guided biopsy[5], which is gold standard for any cervical cancer screening programme and take an adequate biopsy sample (at least 0.5X 0.7 cm) with a small area of normal tissue for better interpretation. A dedicated team of trained colposcopists, along with cytologists and pathologists working in close coordination works very well in countries where there is absence of national screening policy, making referrals for colposcopy, training and continuous practice of the subject exclusively mandatory.

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# Nonavalent vaccine - A new approach

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Human Papilloma Viruses are a group of more than 200 related viruses, of which more than 40 types can spread through direct contact from the skin and the mucous membrane of an infected person. There are two types of human papilloma viruses – low risk and high risk. While low risk viruses like 6 and 11 can cause skin warts on or around genitals, anus, mouth or throat, high risk HPV types can cause carcinomas of the cervix and anus. More than a dozen of these have been identified though HPV 16 and 18 are the ones responsible for most HPV-related cancers. Cervical cancer is the second most common cancer in the world between 20 and 45 years of age[1]. HPV vaccination can serve to reduce the prevalence of cervical cancer in this group.

## Importance of 9 Valent Vaccines

The first vaccine to be licensed was Gardasil in 2006. It is a quadrivalent HPV vaccine which protects against HPV types 6,11,16 and 18. It is composed of virus like particles with assembly of L1 capsid protein obtained from each of the four types. The latest type of vaccine to get FDA approval is Gardasil 9 in December 2014. Gardasil 9 prevents infection with the same four types plus five additional high risk types - 31, 33, 45, 52 and 58. Hence it is called 9 – Valent Vaccine. Gardasil 9 has been approved in females from 9 to 22 years of age for the prevention of high risk viral infection causing cancers, precancerous anal and genital lesions[4]. This vaccine has been approved in males also starting from the age of nine. Data suggest that the antibody titres after vaccination are much higher than after natural infection. This indicates a long term protection although the requirement of booster dose will be clearer after the availability of long term data.

## Mechanism of action

HPV viruses stimulate the body to produce the antibodies and these antibodies subsequently bind to the viruses and prevent it from infecting the body cells and tissues. Virus like particles that are formed by HPV surface components are strongly immunogenic and evoke a strong antibody response. HPV vaccines are highly effective in preventing the infection before the exposure to viruses. Adjuvants play key role in enhancing the immune response elicited by a vaccine. They are used in almost all commercially available vaccines. The most commonly used adjuvant is Aluminium Hydroxide.

## Protection against HPV infection

Oncogenic human papilloma virus infection is the cause of nearly all cervical cancers and a significant proportion of oropharyngeal and anal cancers. In clinical trials Gardasil 9 is found to be 97% effective in preventing anal and cervical cancers caused by the five additional types. Protection is usually for 10-15 yrs[3]. A recent study that closely analysed the adverse reaction of this vaccine shows that these are very similar to those with other vaccines .The aluminium component used in HPV vaccine has an excellent safety record. This vaccine carries a very rare risk of anaphylaxis (1: 200000–300000). So far we don't have sufficient data to suggest adverse events linked to this vaccine.

Anti bodies are an important correlate for long term protection. It is believed that antibody levels that are consistently high over a period of time and are likely to stay high, would provide long term protection against cervical cancer. Further, mathematical modelling suggests that these antibodies are likely to persist for at least 20 years[4]. Studies have also established that these antibodies have highest response at 10 – 15 years of age. Hence, vaccination started at 10 years would afford protection against cancer in future.

A large randomised control study that included more than 15000 patients aged between 16 and 26 yrs of age showed that 9-valent vaccine was determined to be 97% effective as for cervical cancer and 78% effective for anal cancers[4]. This vaccine is administered in 2 shots at 0 and 6 months. High sero-conversion rates and high levels of antibodies are observed in all age groups. This vaccine is well tolerated and an effective means to be able to reduce the burden of anogenital cancers. The cost effectiveness of additional doses of 9 valent vaccine for those who are already vaccinated with 3 doses of quadrivalent vaccine is well established and potential benefit gained in females older than 18 yrs and males of any age is always present[5].

## Indian Scenario

The economic and the social costs of cervical cancer far exceed those of vaccination. Screening is a part of secondary prevention and can only detect lesions after an HPV infection has already started to persist. Screening cannot prevent an HPV infection in the first place.

Currently in India a vast majority of women remain unscreened, and present with cancer at a very late

stage[2]. Vaccination is considered to be primary prevention in that it prevents an oncogenic HPV infection from occurring and persisting[3], thereby reducing the likelihood of it leading to cancer. Screening should continue even after vaccination to ensure that an infection caused by a non vaccine HPV type does not progress to invasive cancer.

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# Journal Scan

Lancet Oncol. 2016 Jan;17(1):67-77.

**Immunogenicity and HPV infection after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre prospective cohort study.**

Sankaranarayanan R, Prabhu PR, Pawlita M et al. Indian HPV Vaccine Study Group.

**BACKGROUND:** An increase in worldwide HPV vaccination could be facilitated if fewer than three doses of vaccine are as effective as three doses.

**METHODS:** Our study was designed to be done in nine locations (188 clusters) in India. Participants were unmarried girls aged 10-18 years vaccinated in four cohorts: girls who received three doses of vaccine on days 1, 60, and 180 or later, two doses on days 1 and 180 or later, two doses on days 1 and 60 by default, and one dose by default. The primary outcomes were immunogenicity in terms of L1 genotype-specific binding antibody titres, neutralising antibody titres, and antibody avidity after vaccination for the vaccine-targeted HPV types 16, 18, 6, and 11 and incident and persistent infections with these HPVs. Analysis was per actual number of vaccine doses received.

**FINDINGS:** Vaccination of eligible girls was initiated on Sept 1, 2009, and continued until April 8, 2010. Of 21 258 eligible girls identified at 188 clusters, 17 729 girls were recruited from 178 clusters before suspension. 4348 (25%) girls received three doses, 4979 (28%) received two doses on days 1 and 180 or later, 3452 (19%) received two doses at days 1 and 60, and 4950 (28%) received one dose. Immune response in the two-dose HPV vaccine group was non-inferior to the three-dose group (median fluorescence intensity ratio for HPV 16 1·12 [95% CI 1·02-1·23] and for HPV 18 1·04 [0·92-1·19]) at 7 months, but was inferior in the two-dose default (0·33 [0·29-0·38] for HPV 16 and 0·51 [0·43-0·59] for HPV 18) and one-dose default (0·09 [0·08-0·11] for HPV 16 and 0·12 [0·10-0·14] for HPV 18) groups at 18 months. Fewer than three doses by design and default induced detectable concentrations of neutralising antibodies to all four vaccine-targeted HPV types, but at much lower concentration after one dose. Cervical samples from 2649 participants were tested and the frequency of incident HPV 16, 18, 6, and 11 infections was similar irrespective of the number of vaccine doses received. The testing of at least two samples from 838 participants showed that there was no persistent HPV 16 or 18 infections in any study group at a median follow-up of 4·7 years (IQR 4·2-5·1).

**CONCLUSION:** Despite the limitations imposed by the suspension of the HPV vaccination, our findings lend support to the WHO recommendation of two doses, at least 6 months apart, for routine vaccination of young girls. The short-term protection afforded by one dose of HPV vaccine against persistent infection with HPV 16, 18, 6, and 11 is similar to that afforded by two or three doses of vaccine and merits further assessment.

Mod Pathol. 2016 Aug;29(8):870-8

**p16/Ki-67 dual-stained cytology for detecting cervical (pre)cancer in a HPV-positive gynecologic outpatient population.**

Luttmer R, Dijkstra MG, Snijders PJ, et al.

Women who test positive for a high-risk type of the human papillomavirus (HPV) require triage testing to identify those women with cervical intraepithelial neoplasia grade 3 or cancer (≥CIN3). Although Pap cytology is considered an attractive triage test, its applicability is hampered by its subjective nature. This study prospectively compared the clinical performance of p16/Ki-67 dual-stained cytology to that of Pap

cytology, with or without HPV16/18 genotyping, in high-risk HPV-positive women visiting gynecologic outpatient clinics (n=446 and age 18-66 years). From all women, cervical scrapes (for Pap cytology, HPV16/18 genotyping, and p16/Ki-67 dual-stained cytology) and colposcopy-directed biopsies were obtained. The sensitivity of p16/Ki-67 dual-stained cytology for ≥CIN3 (93.8%) did neither differ significantly from that of Pap cytology (87.7%; ratio 1.07 and 95% confidence interval (CI): 0.97-1.18) nor from that of Pap cytology combined with HPV16/18 genotyping (95.1%; ratio 0.99 and 95% CI: 0.91-1.07). However, the specificity of p16/Ki-67 dual-stained cytology for ≥CIN3 (51.2%) was significantly higher than that of Pap cytology (44.9%; ratio 1.14 and 95% CI: 1.01-1.29) and Pap cytology combined with HPV16/18 genotyping (25.8%; ratio 1.99 and 95% CI: 1.68-2.35). After exclusion of women who had been referred because of abnormal Pap cytology, the specificity of p16/Ki-67 dual-stained cytology for ≥CIN3 (56.7%) remained the same, whereas that of Pap cytology (60.3%) increased substantially, resulting in a similar specificity of both assays (ratio 0.94 and 95% CI: 0.83-1.07) in this sub-cohort. In summary, p16/Ki-67 dual-stained cytology has a good clinical performance and is an interesting objective microscopy-based triage tool for high-risk HPV-positive women.

BMJ Open. 2016 Apr 25;6(4):e010660.

**Clinical validation of hrHPV testing on vaginal and urine self-samples in primary cervical screening (cross-sectional results from the Papillomavirus Dumfries and Galloway-PaVDaG study).**

Stanczuk G, Baxter G, Currie H et al.

**OBJECTIVES:** Papillomavirus Dumfries and Galloway (PaVDaG) assessed the performance of a high-risk human papillomavirus (hrHPV) PCR-based assay to detect high-grade cervical intraepithelial neoplasia (CIN2+) in self-collected vaginal and urine samples.

**METHODOLOGY:** 5318 women aged 20-60 years provided self-collected random urine and vaginal samples for hrHPV testing and a clinician-collected liquid-based cytology (LBC) sample for cytology and hrHPV testing. All samples were tested for hrHPV using the PCR-based Cobas 4800 assay. Colposcopy was offered to women with high-grade or repeated borderline/low-grade cytological abnormalities; also to those who were LBC negative but hrHPV 16/18 positive. The self-tests' absolute sensitivity and specificity for CIN2+ were assessed on all biospecimens; also, their relative sensitivity and specificity compared with clinician-taken samples. Interlaboratory and intralaboratory performance of the hrHPV assay in self-collected samples was also established.

**RESULTS:** HrHPV prevalence was 14.7%, 16.6% and 11.6% in cervical, vaginal and urine samples, respectively. Sensitivity for detecting CIN2+ was 97.7% (95% to 100%), 94.6% (90.7% to 98.5%) and 63.1% (54.6% to 71.7%) for cervical, vaginal and urine hrHPV detection, respectively. The corresponding specificities were 87.3% (86.4% to 88.2%), 85.4% (84.4% to 86.3%) and 89.8% (89.0% to 90.7%). There was a 38% (24% to 57%) higher HPV detection rate in vaginal self-samples from women over 50 years compared with those ≤29 years.

**CONCLUSIONS:** The sensitivity of self-collected vaginal samples for the detection of CIN2+ was similar to that of cervical samples and justifies consideration of this sample for primary screening.

## ISCCP Activities

CME on Screening & Prevention of Cervical Cancer was organized by Institute of Obstetrics & Gynaecology, Sir Ganga Ram Hospital Under the aegis of Sub-Committee of AOGD (Cervical Cancer Awareness & Prevention) NARCHI, ISOPARB & ISCCP. Dr Mala Srivastava was the Organizing Secretary. About 62 delegates attended the CME which had the stalwarts of cervical cancer and colposcopy speaking on various aspects of cervical cancer prevention.


Cervical Cancer Screening Camp was organised by Department of Obstetrics & Gynaecology, Babu Jagjivan Ram Memorial Hospital on 21st April, 2016. It was attended by 120 patients. Five patients screened positive by VIA/VILI and colposcopy was done for them. Two patients underwent cervical biopsy.

Action cancer hospital organised a Colposcopy workshop every month. The program was for one day which included lectures on basics of colposcopy and management of CIN, followed by case demonstrations.

The workshop was attended by gynaecologists from various parts of India as well as foreign countries. Glimpses from the last four workshops are given here.

CME programme on Diagnostic and Operative Colposcopy workshop was held at Bhopal under the aegis of ISCCP. This meet was presided over by Dr Gauri Gandhi, President ISCCP and Dr Kavita N Singh from Jabalpur. Dr Shraddha Agarwal was the Organizing Secretary. It was attended by 110 eminent Gynaecologists from in and around Bhopal. This included Senior Consultants from Medical Colleges and Private sector. This created an immaculate platform for exchange of knowledge and experiences to benefit women at large.