ICOG FOGSI Recommendations for
Good Clinical Practice

Detection and Management of Pre Cancerous Lesions of the Cervix

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Preamble

Cancer of the uterine cervix is still the commonest cancer among Indian women, although overtaken by breast cancer in certain parts of the country. Of the approximately 500,000 new cases reported world-wide each year, one fourth occur in India.Also, the majority of these patients present in advanced stages, leading to increased mortality and morbidity. 75,000 or more of our country-women will die from this disease every year. Hence India accounts for 26.7% of the incidence and 27% of deaths due to this disease world-wide. This disease is truly a scourge for our countrywomen.

Cervical cancer can be detected in early or pre-invasive stages with the help of screening, thus greatly reducing the morbidity and mortality. In developed countries with an organized Pap's smear screening program on a national level, the incidence and mortality from cervical cancer has been dramatically reduced. However, screening of all women in India is likely to remain an unrealized goal due to various reasons. So far, screening has not been implemented properly and has had no impact on the incidence or death rates in India. Hence some other preventive intervention must be considered.

It has been established that infection with high risk human papillomavirus type is a necessary cause of cervical cancer in almost 100% cases. HPV type 16 & 18 are responsible for 70% of the invasive cervical cancers. Hence a prophylactic vaccine against these HPV types will be able to provide the population wide primary prevention against the disease. This, if implemented properly, could be the more viable and practical option in a country such as ours. However, even for vaccinated persons, screening has to continue. So establishment of screening protocols and facilities for screening have to be organized.

As a result of screening, a large number of precancerous cases will be detected. They will need proper treatment to prevent invasive cervical cancer. Recommendations have to be given out to all the Gynaecologists practicing in India for the same.

Proper treatment of precancerous lesions is the key to the success of Cervical Cancer Control programmes. The protocols for these treatments are known and followed in most parts of the world.

We need to have our own Recommendations. Further we must modify and revise from time to time so as to keep up with the knowledge and development. We must take into consideration that the disease is seen to be more aggressive and seen in advanced stages in practice. Facilities are not available all over and are concentrated in urban centres. The disease is seen more in low socio-economic strata of society, who have limited access to healthcare.1.1

Contents

1. Detection

There is as yet no organized screening programme for the country. Screening was recommended in 1984 when National Cancer Control Programme (NCCP) was launched. Subsequently programme has been revised, the last one being in 2006.

However, it is recommended that women undergo periodic cancer screening based on the following criteriae.

1. **Sexually active women above 30 years of age.**
2. **Sexual life more than 10 years.**
3. **More than 3 pregnancies and labour.**

Screening methods to be used

1. Visual inspection of Cervix with 3% or 5% acetic acid (VIA).
2. Visual inspection of Cervix with Lugol's Iodine (VILI).
3. Pap smears from Ectocervix & Endocervix.
4. Introduce HPV testing whenever possible.
5. Introduce Colposcopy whenever possible.

2. Management

Visual inspection with acetic and (VIA) and visual inspection with Lugol's Iodine (VILI) are 2 simple tests to detect pre cancerous lesions of the cervix.

In VIA, after swabing the cervix with 3% or 5% acetic acid, pre cancerous lesions appear as a white thickned patch. It may be on the cervix or on the vagina.

In VILI Lugol's Iodine is used. Normal epithelium stains dark brown due to the glycogen content. Precancerous lesions appear unstained or as yellow patch. VILI can be performed afte VIA. Both these tests are simple and comfortable to the patient and can be per formed by para medicals. In VILI, the distinction between normal and abnormal epithelium is clearer and easier to note. It also is more acceptable to the patients as it does not cause burning since it is an aquous solution of Iodine. Acetic acid may cause temporary burning. However, VILI has lesser specificity and sensitivity than VIA. Cases undergoing VIA / VILI are Classified as:

- negative
- positive
- suspicious of Cancer

The latter are cases where a frank growth or ulcer or bleeding area is seen.

1. **VIA or VILI positive women**

   about 10-15% women are likely to be tested +ve by these methods.

   Recommended management.

   1. Careful assessment by a Doctor, preferably Gynecological check up.
   2. Treat infection, anemia, nutritional deficiency and follow up.
   3. Advise Pap smear test and treat accordingly.
   4. Consider biopsy and treat accordingly.

   Some VIA cases seen as erosion after abortion or delivery may not require active treatment.

2. Women with abnormal smears

Many terminologies are used in Cytology. The following chart gives a comparative analysis. It is best of discuss with the Cytolpathologist what is the accurate assessment of the degree of abnormality. Currently Bethesda classification is preferred in most parts of the world. Lowgrade squamous intraepithelial lesions are likely to regress and hence may be treated conservatively and kept on follow-up. High grade lesions on the other hand are likely to progress to invasive cancer.

Classification of Squamous Cell Abnormalities

WHO Classification	CIN Grading	Bethesda System (1)	PAP Classification
Normal	Normal	Normal	Class I
Atypia Reactive or Neoplastic	Atypia	ASCUS*	Class II
HPV	HPV	Low-Grade SIL**	Class II
Atypia with HPV	Atypia "condyl omatous atypia" and "koilocytic atypia"	Low-Grade SIL	Class II
Mild Dysplasia	CIN I	Low-Grade SIL	Class III
Moderate Dysplasia	CIN II	High-Grade SIL	Class III
Severe Dysplasia	CIN III	High-Grade SIL	Class III
Carcinoma-in-situ	CIS	High-Grade SIL	Class IV
Invasive Cancer	Invasive Cancer	Invasive Cancer	Class V

* ASCUS: Atypical Squamous or glandular cells of undetermined significance should be qualified further, if possible, as to whether a reactive or neoplastic process is favored.

**SIL: Squamous intraepithelial lesions.

The following are the principals of management.

Patient and her family should not be alarmed by saying that she has the beginning of cancer or is going to develop cancer. Patient must be reassured that "Propre treatment at this stage will prevent the possibility of Cancer". It is also important to inform that at a certain stage all changes are reversible but it requires observation over a period of at least 2 years.

It is also important to treat the patient as a whole and not just "smear". The physician in charge must make a note of patients desire, her social and economic condition and availability of facilities in her geographic area. Improvement in gen health and hygiene and correction of anaemia and use of barrier contraceptive will give protection.

There are some special group of individuals who may need very special care. Some of these are

a. Adolescent Girls. Will need a more conservative approach.
b. Pregnant Women. Will a more conservative approach.

c. Immunocompromised persons
d. Those with other health conditions

As per the smear report, the patients are divided into the following 5 categories. **Squamous metaplasia is physiological change and needs no treatment.**

a. Human Papilloma Virus (HPV) Lesions only.
b. Low Grade Lesions
   1. Atypical Squamous Cells of Uncertain Significance (ASCUS)
   2. Low Grade Squamous Intraepithelial Lesions (LGSIL).
c. High Grade intra epithelial Lesions (HGSIL).
d. Micro invasive or occult invasive Lesions.
e. Glandular Lesions.

a. HPV Lessions only.

1. Evaluation of lower genital tract with acetic acid – preferably by Colposcopy.
2. Follow up for upto 2 years as the infection usually clears up.
3. Reassure the patient and her family. Improve general health, hygiene and nutritional status.
4. At any stage, if CIN or VaIN or VIN developes, treat accordingly.
5. HPV testing if possible.
6. Treat with local therapy.

b. Low Grade Lesions ASCUS and LGSIL

These are essentially reversible. Follow up required for at least 2 years.

1. Full Gynecological check up.
2. Treat infection and repeat smear.
3. HPV testing of possible.
4. Colposcopy of possible.
5. If lesions persists for 6 months or more – further evaluation suggested.
6. or Colposcopically directed biopsy may be considered.

c. Management of HGSIL

1. Endocervical curettage and multiple punch biopsies (only for diagnosis).
2. Colposcopic Evaluation.
3. HPV testing may be done, but it has limited value as 80 – 90% will be positive.
4. Local Excision is mandatory for diagnosis. In some cases it may be therapeutic.

- Cone Biopsy
- LEEP / LLETZ after colposopic evaluation.
- CO_2 Laser conisation after colposcopic evaluation.

Further treatment will depend upon the histopathology of the specimen excised.

Primary treatment by Hysterectomy without excluding micro or early invasion is not acceptable.

Post cone / leep if diagnosis is confirmed, patient is categorized into 3 groups.

Group I — Margins are free of disease. Life long follow-up is recommended. Patient and family are informed that the risk of developing cancer is 2.34 times greater especially in women over 50 years of age.

May consider hysterectomy as an option.
Especially if age is > 40 years.
Family is complete.

Group II — Margins are free of SIL but not of HPV
- Close follow up.
- HPV testing if possible.
- Hysterectomy

Group III — Margins are not free of SIL
- Repeat deeper cone
- Hysterectomy

d. Micro invasive or occult invasive diagnosed on excisional tissues

Gynaecologist may treat following FIGO guidelines.

e. Glandular Lesions

These cells may be from endocervix, endometrium, fallopian tubes or ovary.

1. Full clinical examination.
2. Endocervical and Endometrial sampling.
3. Ultrasound Scan.
4. Fractional curettage / hysteroscopy or laparoscopy.

There is a high potential for malignancy in symptomatic women. No time should be lost. Reference to a suitable center may be considered.

3. Conclusion

Proper treatment and management of precancerous lesions will prevent invasive cervical cancer and “Save Lives”. There should be neither under treatment nor over treatment. Menstrual, sexual and reproductive functions need to be preserved in young women. However, the fear of Cancer looms large and patients seek drastic treatment. Hence “Counselling” will remain an essential component of treatment.

Diagnosis and management of pre cancerous lesions forms a part of “Secondary Prevention” strategy. It has been used extensively in the developed world for the last 50-60 years and has given excellent results. The incidence and mortality of cervical cancer have come down.

However, today, primary prevention by using HPV vaccines is available in most parts of the world and also in India. Screening has to continue even for vaccinated women.

Therefore we must simultaneously use primary and secondary prevention strategies for the control of cervical cancer.

4. Recommended Reading

- Outlook. Preventing Cervical cancer : Unprecedented Opportunities for Improving Women's Health.
  www.path.org/publications/details.php?I=1508
- Cervical Cancer, human papillomavirus (HPV), and HPV vaccines : Key points for policy- makers and health professionals (WHO, PATH, UNFPA).
  www.rho.org/files/WHO_PATH_UNFPA_cxca_key_points.pdf
- Alliance for Cervical Cancer Prevention
  www.alliance-cxca.org
- Evidence of Developing Country Support for Improved Cervical cancer Prevention
  www.rho.org/CCAdossier.
- World Health Organization Cervical Cancer resource page
  www.who.int@reproductive-health/publications/cancers.html
- International Agency for Research on Cancer
  www.iarc.fr