Guidelines for Cancer Screening for Women in India

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Cancer screening in gynaecology is a recent phenomenon. It is only since the middle of the 20th century that the concept of doing a check up on normal healthy women with the aim of finding an early asymtomatic cancer has been accepted in gynaecological practice.

Defenition and types of screening

Screening is defined as 'the presumptive identification of unrecognised disease by the application of diagnostic procedures which can be applied rapidly and safely'. The screening tests used are designed to sort out apparently well persons from those who are probably harbouring the disease. However, it is important to recognise that the sceening tests are not intended to be fully diagnostic. Further evaluation of the case is necessary.

Mass screening is an extension of the screening activity conducted on the whole population or a major subgroup, for example, all adults. Selective screening conducted on a segment of a population at relatively high risk. High risk groups can be identified by previous epidemiological studies. Mass screening is expensive, and therefore when resources are limited, selective screening may be resorted to. 'Multiphasic screeing' is when a person can be screened for several conditions at the same sitting: for example, breast and genital tract cancers. This reduces the cost of screening. 'Opportunitic screening' is the screening of those attending the hospitals for any complaint. It has been found to be very useful. The case is strong to implement it in the initial stages of any screening programme.

Cancer screening in gynaecology includes screening mainly for 1. Cervical cancer 2. Endometrial cancer 3. Ovarian cancer and 4. Breast cancer. Other cancers such as vaginal and vulval cancers are very rare and hence screening for them is generally not included in routine screening programmes.

Cancer screening is also the domain of preventive and social medicine. Today, the emphasis everywhere is more on prevention and hence the concept of cancer screening has gained a lot of importance.

A lot of fundamental and clinical research has been undertaken on cancer in the last few decades. This has led to the better understanding of the course of development of cancer and its precancerous phases. Moreover, the role of carcinogens and cocarcinogens have been clarified.

Cervical Carcinoma

The natural history of cervical cancer is favourable for effective screening. It has now been proved beyond doubt that invasive cervical cancer is the end result of a process of carcinogenesis which starts at its earliest stage with inflammatory change. If the carcinogen keeps acting on the cells they undergo a series of changes of mild, moderate and severe dysplasia, then on to carcinoma-in-situ and finally to invasive cancer.

Normal Cell
Inflammation
Mild dysplasia
Moderate dysplasia
Severe dysplasia
Carcinoma-in-situ Invasive Cancer
Invasive Cancer

The carcinogen involved in cervical cancer is not yet identified. It may be the smegma (from the male partner), a virus (human papilloma virus or Herpes genitalia virus - HSV-II) or may be a chemical. Much depends on the host response. If the host response is good, the carcinogenesis is arrested at an earlier stage. The factors responsible for host response are also not known but genetic background, nutritional status and life styles including sexual behaviour may play a role.

Cytologic Screening for Cervical Cancer

Before a Pap smear is obtained, the woman should abstain from coitus or vaginal douching for at least 24 hours. No intravaginal medications are advised for a week before the test. A lubricant is avoided during the examinations. The smears collected and stained are interpreted as 1. Normal, 2. Atypical, 3. Dysplasia mild, moderate and severe, 4. Carcinoma-in-situ, and 5. Invasive squamous cell carcinoma or adenocarcinoma (WHO system).

Abnormal Cells are seen as shown is (Fig. 1).

1. **Mild dysplasia:** The cells are generally of the intermediate or superficial type. There is a slight nuclear enlargement with mild hyperchromasia. Binucleation is common.

2. **Moderate dysplasia:** Here the cells are mostly of the intermediate type. They show moderate nuclear enlargement with hyperchromasia and irregular chromation pattern. Multinucleation may be seen.

3. **Severe dysplasia:** The cells are of the parabasal type showing an increased nuclear cytoplasmic ratio. The nucleus is irregular with coarse chromatin pattern. Scanty or only a rim of cytoplasm is seen.

4. **Carcinoma-in-situ:** The cells are of the parabasal type showing a high nuclear - cytoplasmic ration. The nucleus may be round or oval with an irregular nuclear margin and a finely granular to coarsely granular chromatin pattern. Very scanty or hardly any cytoplasm may be seen.

5. **Invasive cancer:** The cells here are seen singly but are often grouped as syncytial masses. Cells show irregular nuclei which may be small or large. The nuclear chromation is irregular coarse. Nucleoli are often encountered. Large nonkerratinising cells or well differentiated fibre cells or tadpole cells are seen.

6. **Adenocarcinoma** : The Cells are of glandular origin. They are seen in groups or compact clumps with eccentric irregular nuclei containing large prominent nucleoli. The cells are round or columnar.

In cases of carcinoma-in-situ, the background is normally clear. In cases of invasive cervical cancer, the background is necrotic.

In 1988, the Bethesda system of reporting the cervical cytological smears was suggested (Table 1) but has not been universally accepted. It gives the gynaecologist less information than the other methods of reporting. However it is gaining acceptance.

Table : 1

Classification of Cervical Smears

Papanicolaou's	WHO system	Bethesda

Concept of down-staging of cervical cancer.

Down staging of Disease

Unfortunately in India, women come much too late when the cancer is incurable and no treatment is available. However if women were to come early, the diagnosis can be made in the first and second stage. If this is done, the mortality will come down immediately.

Down staging involves a periodic gynaecological examination along with education of the women about danger signals. An annual gynaecological check up will eliminate all late cases. The best person to do this is the gynaecologist but others can also be trained to undertake a speculum examination of the cervix.

In Rural cancer Registry at Barsi, down staging of cervical cancer was done by informing the population about the symptoms of invasive cancer. Trained health workers visited all the villages educating the women. Those with symptoms were brought to the Cancer Hospital for a check up (Jayant 1989).

Screening for cervical cancer by visual inspection is re-

ported by Singh et al (1992). In women with abnormal looking cervix the prevalence of cancer was 29/1000 whereas in women with normal looking cervix it was 1.53/1000. They conclude that the yield for cancer is very high if women with symtoms and abnormal looking cervix are screened by cytology.

To control a disease one must know its etiological factors and be in a position to eliminate them and thus bring down the incidence. This is called primary prevention. Secondary prevention involves the treatment of its premalignant phase.

Cervical cancer is considered a preventable disease by WHO. This is because it can be diagnosed in its precancerous phase. Therefore, it is disease which can be controlled. This has been achieved in most parts of the developed countries. The incidence has come down and so has the mortality. Out of all cervical cancer cases seen in the world 14 per cent are in the developed countries and about 86 per cent occur in the developing countries (Miller, 1986).

Although all etiologic factors are not known, it is a disease related to sexual activity (Lulla and Saraiya, 1983). The contributory risk factors are sexual behaviour - a) age at commencement of sexual activity, number of partners, b) multiparity, c) sexually transmitted deseases especially HPV and PID, d) low socio-economic groups, and e) type of contraceptive practice-more with pill users than those using barrier contraception. The high risk women should be screened annually.

To be effective, the screening should be sensitive, specific, cost effective, acceptable and cover the risk groups. There should be good quality control and liason with general practioners.

In a study of over 92,000 women screened at the author's institution in Bombay over a 20-year period, the pick-up rate of abnormal smear was 14 per 1,000 (Table 2). There were 88 cases of occult invasive carvinoma detected by clinical evaluation. In the same period, 870 cases of invasive cervical carcinoma were seen indicating that the disease is widely prevalent in the community.

Table :2

Other methods of Screening for Cervical cancer.

Besides cytological screening, cervical carcinoma can be detected by visual inspection of cervix including:
1. Colposcopy, and 2. Cervicography.

Colposcopy : Though colposcopy is useful in identifying the lesions in the transformation zone, the endocervical lesions are likely to be missed. It is not as sensitive as cytology in detecting early invasive cervical carcinoma due to the difficulty in identifying abnormal vessels (Lohe et al, 1978). But it is extremely useful in the evaluation of women with abnormal cytologic smears. As a screening procedure, it is labour intensive, costly and has a low specificity (Wilkinson, 1990).

Cervicography: This is a photographic screening technique in which a 35 mm picture is taken of the cervix after applying 3-5 per cent acetic acid and the resultant film is projected onto a screen to give an enlarged view of the cervix (Stafl, 1990), In this programme, the projection and interpretation are centralised. In the limited trials, cervicography is reported to have a sensitivity as high as 94 per cent but specificity of only about 50 per cent (Campion et al, 1990). It may be of use in cases of a typical smears in areas where colposcopic facilities are not available.

Endometrial Carcinoma

The developmental concept for carcinoma of the body of the uterus has not changed much since Cullen described it in 1900, almost a hundred years ago. He had clearly indicated that it began with anovulatory cycles. The changes occurred as follows:

Anovulatory bleeding
Cystic glanular hyperplasia
Adenomatous hyperplasia
Adenocarcinoma - in - situ
Invasive adenocarcinoma

How long the changes will take to progress and at what

stage the lesion is reversible are some of the questions which remain unanswered. Although, all cases may not progress in this manner, the fact that a precursor stage exists and can be diagnosed is reason enough to justify screening.

What has been changing, however, is the clinical pattern of the disease. It is known to be a disease of the postmenopausal women occuring after the age of 50. However, now it is seen to occur frequently in premenopausal women as well. The racial variation is still the same, the lesion being more common in the white caucasian populations than in the black or negroid races.

In the developed countries, the ratio of endometrial carcinoma to cervical carinoma is distinctly changing. It was 1:14.8 in 1930 (Hinselmann) and had come down to 1:1 in 1962 (Gore and Hertig) and by 1986 it was reversed to 2.3:1 (Lacy, 1987).

In Sweden, carcinoma of the breast is the number one cancer in women followed by cancer of the endometrium, and cancer cervix comes third. In India, the cervix continues to be the commonest site of cancer in women and endometrial carcinoma is rare. The ratio of endometrial cancer to cervical cancer is 1:25 (Roy Chowdhury, 1975).

With vaginal cytology, the diagnostic accuracy for endometrial carcinoma was much lower than for carcinoma of the cervix. It was 70-75 per cent (Van Haam, 1958). Torres et al (1969) reported a positivity rate of 95 per cent for endometrial carcinoma with endometrial aspiration compared to only 50 per cent with cervicovaginal cytology. The screening for endometrial cancer can be done by periodic endometrial aspiration and staining by the Papanicolaou technique. If abnormal endometrial cells are detected, the patient is advised fractional curettage and further evaluation. For cancer detection by endometrial sampling, a disposable suction device using Karman's plastic cannula and syringe or vibra aspirator have been described. When endometrial sampling was done in a series of symptomatic women, the sensitivity for detection of endometrial hyperplasia 58 per cent and with a false positive rate of 7.3 per cent. In 1969, Gravlee reported that with a jet washer, the diagnostic accuracy of endometrial sampling could be improved to almost 100 per cent. Using the jet washer, the detection rate of endometrial carcinoma in a group of asymptomatic women, however, was 0.9 percent (Chambers, 1992).

The screening for endometrial cancer has not become as popular as the cytologic screening for cervical cancer. It has not been used to screen large populations. However, it is recommended annually for cases who are at high risk for endometrial carcinoma, e.g., postmenopausal women who are obese, diabetic, hypertensive and with or without fibroids, Also women on oestrogen replacement therapy and those with known history of glandular hyperplasia or family history of endometrial cancer may benefit by such a screening programme.

Ovarian Carcinoma

There is no premalignant phase for ovarian carcinoma. When it is clinically diagnosed, most cases are in advanced stages of the disease and therefore of all female genital cancers, the prognosis is worst in ovarian carcinoma in spite of surgery or multidrug chemotherapy.

In healthy women, periodic gynaecological examination may help in detecting a suspicious adnexal mass which could be subjected to ultrasonography or laproscopy.

Of late, routine ultrasonography has been tried in some women to detect early ovarian carcinoma. Routine transvaginal ultrasound in women over 40 years is advocated by De priest and Nagell (1992). On ultrasound screening, the volume of the ovaries is calculated. If it exceeds 8.0 cc, the ovaries are considered abnormal and transvaginal ultrasound is repeated four weeks later. If still found to be enlarged, laproscopic evaluation with a view to a laparotomy should be performed. If negative, the scan is repeated annually. In a series of 1,300 patients routine transvaginal ultrasound has helped in diagnosing two cases of Stage I ovarian cancer. In 5,500 women screened by abdominal ultrasonography, five cases of Stage I ovarian cancer were diagnosed (Campbell et al, 1989). Ultrasonography at periodic intervals therefore is useful for screening of ovarian cancer. More recently, with the availability of colour flow mapping and Dop-

pler facilities, vaginal ultrasonography may prove effective detecting ovarian cancers in its early stages. However, it is expensive, needs sophisticated machines and expertise, and its specificity is yet to be evaluated. It is unlikely that it would be cost effective for population screening.

Tumour Markers

Of late, tumour markers have been found useful in the management of patients with gynaecological cancer. In cases of gestational trophoblastic disease, the hCG is undoubtedly very sensitive and helps in the early diagnosis and follow-up after therapy. CA-125 is more useful in the diagnosis of pancreatic carcinoma rather than ovarian carcinoma. It is also found in cancer breast, lung and colon. About 1-3 per cent of clinically apparent epithelial tumours of the ovary (especially the nonmucinous type) are associated with elevated levels of CA-125 (Mischell, 1987). But it is not a specific tumour marker as it may be also seen in cases of endometriosis (Kabayashi et al, 1987). Therefore it is not particularly useful in the screening for ovarian cancer, though it may help in monitoring therapy in those cases where it was positive. In the rare endodermal sinus tumour of the ovary, alphafeto protein (AFP) may be detected in the serum. The squamous cell carcinoma antigen (SEG) levels are elevated in most patients with cervical carcinoma but at an advanced stage (Berscnuch et al, 1992). Inhibin, a peptide hormone normally produced by ovarian granulosa cells is not detectable in the serum of menopausal women. It is a useful marker for diagnosis and follow-up of granulosa cells tumours maximal concentration reached is 30,000 IU / litre (Lappohn et al, 1989).

Computerised tomography and magnetic resonance imaging are useful tools in planning treatment than for screening of gynaecological cancers. (Russel et al, 1992). It will be far too costly and therefore not be appropriate for any population screening programme.

Conclusion

Cancer screening in gynaecology today is an important component of health care, and is the responsibility of all gynaecologists, administrators, public health personnel and governments.

There are about 5.9 million cancer cases in the world today. Out of these 2.9 million are in the developed countries and three million in the developing countries since the population of the developing countries is much more than that of the developed countries, the incidence of cancer is lower in the developing countries.

However, this is going to change with rapid industrialisation, increased longevity, changes in life style and continued use of tobacco and other carcinogens. Since the incidence is going to rise, it is necessary to institute screening programmes atleast for the high risk groups.

In India, there are three hospital based and three population based cancer registries. The results show that cancer of the oral cavity in both sexes and cancer of the uterine cervix in women are the commonest malignancies seen in the country. It is estimated that in India the number of cancer cases in women will increase from 0.32 million in 1991 to 0.42 million by 2001 AD, with cancers of the cervix and the breast being major problems (Murthy et al, 1990).

The incidence of cancer cervix (ICD 9-180) is showing a downward trend.

In Madras the incidence is the highest. In 1982 it was 41.6, rose to 48.5 in 1985, thereafter it is showing decline 41.5 in 1991 and 34.2 in 1994.

In Bangalore it was 35.6 in 1982 and 29.5 in 1985. Thereafter it is recorded as 32.2 in 1988, 30.1 in 1991 and 25.5 in 1994.

In Barsi, a rural registry was started only in 1988 when it was 21.4. In 1991 it was 32.7 and 1994 it was 29.

In Bombay the figures have been much lower as the Breast Cancer (174 Breast AAR 27.5 in 1995) is number one. Cancer cervix is number two cancer in women (180 cervix 15.7 in 1995). (Cancer registries ICMR).

The incidence was 18.5 in 1982 rose to 19.3 in 1985. Thereafter it has remained at 21 from 1988 to 1991 and come down to 18 in 1994 and reported to be down to 15.7 in 1995. (Cancer registries ICMR).

It is in areas of high incidence that screening has to be intensive. Apart from screening, attention must be paid to primary prevention or eradication of etiological factors. Improvement in general health, control of fertility and sexually transmitted diseases, and better sanitation are factors which will control the disease.

Augumenting existing facilities for treatment, setting up of detection centres in the periphery and human resources development to carry out the programmes are the goals which will make cancer screening a reality in the future.

Although screening and detection of cancer of the breast in its early stages should come within the realms of screening for gynaecological malignancies and fall with in the responsibility of the gynaecologist, it is considered separately under "breast cancers" because of the increasing incident and high mortality associated with the disease. (Refer to chapter on "Breast cancer").

Guidelines for Fogsi Members

1. Create awareness about cancer in your patients. Keep them informed about symptoms of cancer.
2. Do not frighten, but enlighten.
3. Encourage your patients between the ages of 35-60 to come for annual gynaecological examination. You must do downstaging in your own practice. No one should come with stage III and stage IV. That must be your aim.
4. In addition to PV exam, do a careful PS examination with a good light. If possible paint with either 3% acetic acid or Schiller's Iodine
5. If any suspicious lesion is seen, go ahead for cytology and or biopsy.
6. In Perimenopausal bleeding cases, suggest a pelvic USG scan and note the endometrial thickness. If more than 6mm/suggest endometrial aspiration cytology or an OPD endometrial biopsy / hysteroscopy.
7. In cases of high risk of endometrial cancer suggest endometrial sampling.
8. All cases of perimenopasual irregular bleeding should be treated with D&C. All cases of hyperplasia and or polyps to be evaluated carefully and advice the long term followups.
9. Teach your patients to do Breast Test Examination. Do a breast palpation at the time of annual checkup. Male gynaecologists should be careful. Do this only in the presence of NURSE.
10. Keep promotional literature available in your clinic.
11. If you have a very busy practice, keep a time free say once a fortnight for conucting a "Special Health checkup Clinic".
12. Keep in touch with your cytologist.
13. Put up a Board saying "Cancer checkup available."