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Review Articles

Cervical Precancer: Evaluation and Management

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Abstract

Carcinoma of the uterine cervix is one of the leading cancers among women in our country. This invasive disease is preceded by a number of precancerous conditions detectable by a cytological screening method called as Pap smear. If the precancerous changes in cervical tissue (which can linger for years) are identified and successfully treated, the lesions will not develop into cancer. So, the pathway of preventing cervical cancer deaths is simple and effective. The present article describes the recent ideas about classification and management approach of these precancerous lesions.

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Introduction

Cervical cancer is the most common malignancy in women and is undoubtedly the only cancer that is potentially preventable. Global efforts to prevent the disease have focused on screening women using Pap smears (named for inventor Dr George Papaniculaou) and treating precancerous lesions. Pap smear screening, also called cytological screening, has achieved impressive results in reducing cervical cancer incidence and mortality in some developed countries. But in developing countries like ours, where approximately 80% of all new cases occur-many women have never had a Pap smear. A well planned cytological screening program with an intensive infrastructural support is essential to reduce the incidence of this preventable disease in our country. Most if not all, cases of preinvasive and invasive cervical disease are caused by human papilloma virus, which is spread by sexual contact. The virus infects cells in the transformation zone, the junction between the ectocervix and endocervix, causing nuclear atypia, dysplastic-appearing cells and in rare cases, cancer. Early precancerous changes can be detected by cervical Pap smears and effectively treated. To achieve this a system of adequate follow-up must be established.

Pap smear–an overview

A Pap smear is a cytological test designed to detect abnormal cervical cells. The procedure involves scrapping cells from the cervix and then smearing and fixing them on a glass slide. Slides are then evaluated by a competent cytologist who determines the cell classification.

The Pap smear is generally considered to be a very specific test for high-grade lesions or cancer. Sensitivity is the proportion of women correctly identified by the test as having these conditions. The accuracy of a normal (or negative) cervical smear result, if the specimen is properly taken and reliably screened and interpreted, gives good protection against development of cervical

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cancer within the next three to five years, but it does not completely exclude the presence of small areas of usually low grade CIN.[2] Colposcopic examination and cervicography are more sensitive tests for CIN, but they are not practical screening procedures, because they are too sensitive and would involve too many women in largely unnecessary investigations and treatment for small mostly low grade CIN and HPV infection. In general, it is not possible to increase pap smears. While these approaches appear promising, they are expensive and rely heavily on technology.[3, 4]

Screening Recommendations

A. Whom to test

* All women who are sexually active.
* All women over eighteen years of age.

B. When to test

* The patient should not be actively menstruating[5].
* Smears are best taken at mid menstrual cycle when the cervix is slightly paulous[6].
* It is preferable that the patient refrain from sexual activity or use of vaginal medications for the 48 hours prior to the test.

C. How often to test

* **High-risk women**[5, 7] should have a Pap test every year.
* High risk women includes-
  a) A history of early coitus (Younger than age 16)
  b) Multiple sexual partners or partners with multiple sexual partners.
  c) Sexually transmitted diseases like HIV.
  d) History of condyloma.
  e) Prior abnormal Pap.
* **Women who are not at High risk** for cervical cancer should have a Pap test every year until they have three consecutive normal Pap test. At a minimum all women should have a Pap test every three years.

Pap smear classification system

One of the big difficulties in discussing Pap smears is the mixing and matching of different classification systems that have been used through out the years. The first system was a "Class" system and that was followed by a "Dysplasia" system. Then came a "CIN" classification and finally the currently used "Bethesda" system. It often takes years, however, for pathologists and clinicians to make full transitions to the new terminology without including terminology from or referencing to past classification systems. To better guide the treatment of precancerous cervical changes, a simplified system of classifying these early lesions- the Bethesda system has been established in 1991. A more refined form of this system –the Bethesda 2001 Pap smear classification system has been introduced very recently. A comparison of the different terminologies (Table-1) and the most recent system (Table-2) are shown in the tables below.

Table-1: Terminology for Cervical Abnormalities: A General Comparison.

The Bethesda System (TBS-1991)	Cervical intraepithelial Neoplasia (CIN) System	Common Dysplasia terminology
Atypical squamous cells of undetermined significance (ASCUS)	Cellular atypia	Unspecified cellular changes
Low grade squamous intraepithelial lesions (LSIL)	CIN I	Mild dysplasia
High grade squamous intraepithelial lesions (HSIL)	CIN II	Moderate dysplasia
HSIL	CIN III (includes carcinoma in situ [CIS])	Severe Dysplasia/CIS

Table 2. The Bethesda System-2001 (TBS-2001) Pap Smear Classification System

Bethesda 2001-Epithelial cell Abnormality	
SQUAMOUS CELL	*GLANDULAR CELL*
Atypical squamous cells Atypical squamous cell changes of undetermined significance ASC-US cannot exclude high grade intraepithelial lesion ASC-H **LSIL-** Low grade squamous intraepithelial dysplasia encompassing: HPV/mild dysplasia/CIN 1 **HSIL-** High grade squamous intraepithelial dysplasia encompassing: moderate or severe dysplasia, CIS/CIN-2, CIN-3 with features suspicious for invasion (if invasion suspected)	**Atypical** - endocervical cells - endometrial cells - glandular cells **Atypical** - endocervical cells, favor neoplastic - glandular cells, favor neoplastic Endocervical adenocarcinoma in situ - Adenocarcinoma - endocervical - endometrial - extrauterine - not otherwise specified
Squamous cell carcinoma	Other malignant neoplasms/cancer

The Bethesda system (TBS) 2001 workshop, sponsored by the American society of clinical Pathology (ASCP) brought together 500 cytopathologists, cytotechnologists, clinicians and patients advocates from over 20 different countries in Bethesda, Maryland, USA; April 30, to May 2. Participants gathered to develop this uniform terminology for the reporting of cervical cytopathology results.

The major Part of this recent classification (Includes epithelial cell abnormalities only) is quoted below-

Current Management Approach

With the strengthening of cytological screening programs, pre-malignant lesions of the cervix are being increasingly identified. These need to be treated effectively for any real impact on cervical cancer incidence and mortality. As with any screening test, the actual microscopic changes in the cervical tissue can be worse than the cells picked up on pap indicate or they can be the same or even less abnormal. To tell what the actual changes are, a cervical biopsy is needed in which the tissue is viewed under the microscope. Doctors, however, should not always recommend cervical biopsies for abnormal Pap smears because of the abnormal Paps will regress to normal on their own.[5]

Some key points are described below for a better management of precancerous lesions.

Squamous cell Abnormality

1. ***ASCUS (Atypical squamous cells of undetermined significance)***--- The test should be repeated at 4-6 months interval until three consecutive normal Pap smears, then return to annual screening.[5, 9]

If any repeat smear reveal ASCUS, Patient should be referred to a Gynaecologist for colposcopy.

2. ***LSI L (CIN-I or mild Dysplasia, and/or HPV cytopathic changes)*** should have a repeat smear after 3-6 months in an asymptomatic woman. If the same grade of abnormality persists for two or three smears, referral for colposcopy is indicated[6, 10] HPV lesions may regress spontaneously, persist for long periods

but about 30% of such lesions will progress to CIN within 6-18 months.[9] It is important to be aware of the relatively poor sensitivity of the smear test in the presence of invasive cervical cancer and to advice examination by a Gynaecologist even for a mild dyskaryotic smear if there is abnormal bleeding or discharge[11]. It should also be kept in mind that a small proportion of LSIL might reveal HSIL on colposcopy[7]. Hence in symptomatic patients immediate colposcopy and biopsy is indicated.

3. ***HSIL (CIN II or moderate Dysplasia, CIN-III or severe Dysplasia)*** should go for colposcopy and biopsy. Once diagnosed all High-Grade lesions must be treated either with local destruction (ablation) or excision (Provided removal of all pathological tissue is assured). Hysterectomy in HSIL lesions is mainly indicated in older, non-compliant patients, or those with co-existent uterine pahology.[5,9,12]

Glandular cell Abnormality

AGCUS (Atypical glandular cells of undetermined significance)

Atypical endocervical or endometrial cells favoring reactive changes should go for colposcopy[7].

* Atypical glandular cells favoring neoplasia should undergo colposcopic biopsy.[5,7,9]
* All patients treated for premalignant lesions of the cervix require follow-up cytology and colposcopy at 3,6 and 12 months and thereafter annually.[12]

FEW WORDS ABOUT COLPOSCOPY AND CONE BIOPSY

The use of colposcope allows the clinician to examine the cervix under magnification and to make a directed biopsy. With satisfactory colposcopy, the prediction values of the directed biopsies are excellent.

In our country however, colposcopic facility is not available everywhere and in that case a diagnostic cone biopsy is indicated. Though cone biopsy carries a risk of morbidity and complications in the patient it is the major diagnostic and preventive measure to be adopted at present in our set up.

Cone biopsy has got few other indications also-

i) Unsatisfactory colposcopy- where the cervical transformation zones is not visible.

ii) When a colposcopic biopsy has a lower grade of abnormality than the cytology and colposcopy.

iii) When Endocervical Adenocarcinoma is suspected.

In our country, no effective screening program is available till now and treatment options are also very limited. To develop an effective barrier to the disease a strong infrastructural setup for screening and management is necessary. As cervical carcinoma is the only cancer that is potentially preventable and as this is the leading cause of death from cancer among our women; we should take immediate measures to reduce the incidence of this preventable disease.

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