

Spectrum of Abnormal Cervical Lesions and its Cytohistological Correlation: a Study from an Institute of National Importance of Western Rajasthan

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ABSTRACT

Objective: Cancer of the cervix is the second most common cancer in women worldwide. It accounts for 12% of all cancers in females. Our study aims to find out the pattern of cervical cytology on Papanicolaou smear (Pap smear) and its correlation with histopathological findings in the tertiary care referral centre of Western Rajasthan.

Materials and methods: This is a prospective study carried out over two years, in which all cervical cytology smears were reported as per the 2014 Bethesda system and abnormal cytology was correlated with histopathological findings in cases where cervical biopsy or total hysterectomy specimens were available.

Results: A total of 2291 cervical cytology smears were studied concerning age group, clinical signs and symptoms, and cytology findings. Cervical biopsy correlation was done in 65 patients aged 31–45 (45.61%) years. The mean age of our patients was 41 years. Among the 2291 smears, 181 were unsatisfactory for evaluation. In total, 1982 (86.51%) smears were negative for intraepithelial lesion and malignancy (NILM). Out of 61 abnormal smears, atypical squamous cells of undetermined significance (ASC-US) were seen in 26 (42.62%) cases, atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion (ASC-H) in nine (14.75%) cases, low-grade squamous intraepithelial lesion (LSIL) in four (6.56%) cases, while nine (14.75%) cases were positive for high-grade squamous intraepithelial lesion (HSIL). Invasive squamous cell carcinoma was seen in seven (11.48%) cases and two (3.28%) cases were positive for adenocarcinoma. Atypical glandular cells of undetermined significance (AGUS) were diagnosed in four (6.56%) cases. In our institutional study, specificity was 81.58% and sensitivity 83.33%. The cyto-histopathological correlation was 68.18%, with HSIL (88.89%) having the highest correlation.

Conclusion: Various new techniques have emerged in the diagnosis of a range of lesions of the cervix but as these technologies are costly, they cannot be implemented in poor set up countries. In the present scenario, the Pap smear test is considered the best screening method for cervical carcinoma. Biopsy is always considered to be the gold standard for carcinoma cervix provided that it is taken from representative areas.

Keywords: Papanicolaou smear, abnormal cytology, histopathology.

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INTRODUCTION

Cervical carcinoma is one of the global health problems. Worldwide it is considered the second most common cancer in women. Including India, it is one of the leading causes of death from cancer in several developing countries. According to one of the studies by Anuradha *et al*, the worldwide incidence of cervical cancer is approximately 510,000 new cases annually, with approximately 288,000 deaths worldwide. It usually occurs in middle aged persons and is most commonly found in women over 40 (1). Cancer cervix is easy to cure if it is diagnosed at an earlier stage. Screening of cervical cancer with Papanicolaou/Pap test has significantly reduced the incidence of cervical cancer (1, 2). Early sexual activity, multiple sexual partners, low socioeconomic condition and human papilloma virus (HPV) are considered major risk factors for carcinoma cervix. Human papilloma virus, mainly HPV 16 and 18, herpes simplex type 2 infection and cytomegalovirus are responsible for more than 70% of all cervical cancers (3).

Cytology and histopathological correlation is a widely accepted method of internal quality assurance and it helps in the analysis of various factors leading to discrepant diagnosis. It is possible to detect and diagnose the disease at an earlier stage with the help of cytopathology (4). Our study aims to find out the spectrum of cervical cytology and its correlation with clinical and histopathological findings in a tertiary care referral centre. □

MATERIAL & METHODS

This study is a prospective hospital-based study conducted over the period of two years in the Department of Obstetrics and Gynecology in collaboration with the Department of Pathology of the tertiary care centre of Western Rajasthan, India. All Pap smears within this period were included in the present study. Patients with a history of previous hysterectomy and antenatal women were excluded from the study. Patient data, including name, age, clinical complaints, and per vaginal findings, were collected from the requisition form. For conducting the study, approval was obtained from the Institute Ethics Committee. Pap smear was reported using the

2014 Bethesda system. Abnormal cytology correlation was done with histopathological findings in cases where cervical biopsy or total hysterectomy specimens were available.

Statistical analysis

Statistical analysis was carried out using the SPSS, version 22. The sensitivity, specificity and positive predictive value of the Pap smear test were calculated. Histopathology diagnosis of cervical biopsy was considered the gold standard. □

RESULTS

In the present study, a total of 2291 cytological smears were studied considering the age group, clinical signs and symptoms, and cytology findings. Cervical biopsy correlation with cytological smear was done in 65 cases.

Age distribution in our study

In our study, patients' age ranged from 21–70 years old. Among all patients, 45.61% were in the age group of 31–45 years. The mean age of our participants was 41 years.

The most common symptom found in our study was the whitish discharge per vagina, followed by pain in the lower abdomen, intermenstrual bleeding and dyspareunia.

Cytological diagnosis

A total of 2291 women underwent a cytological examination. Out of those, 181 smears were found to be unsatisfactory for evaluation, 1982 (86.51%) smears were negative for intraepithelial lesion and malignancy and 61 smears had an epithelial cell abnormality (ECA) (2.66%). Among participants with abnormal smears, 26 (42.6%) cases were reported as atypical squamous cells of undetermined significance (ASC-US) (Figure 1a), eight (14.75%) cases as atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H) (Figure 1b), four (6.56%) cases as low-grade squamous intraepithelial lesion (LSIL), nine (14.75%) cases as high grade squamous intraepithelial lesion (HSIL) (Figure 1 c), seven cases (11.48%) as invasive squamous cell carcinoma (Figure 1 d), and two (3.28%) cases were identified as adenocarcinoma. Atypical glandular cells of undetermined significance (AGUS) were found in four (6.56%) cases. In the inflammation category, bacterial vaginosis was the

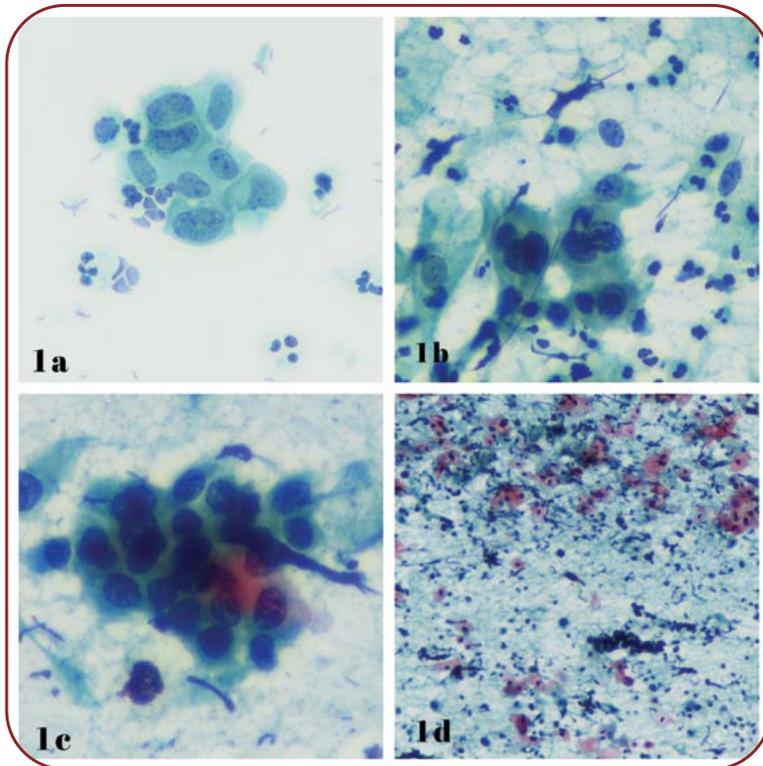


FIGURE 1. (a) Pap smear conventional type 40X ASCUS; (b) ASC-H; (c) Pap smear conventional type 40X HSIL; (d) 10X SCC

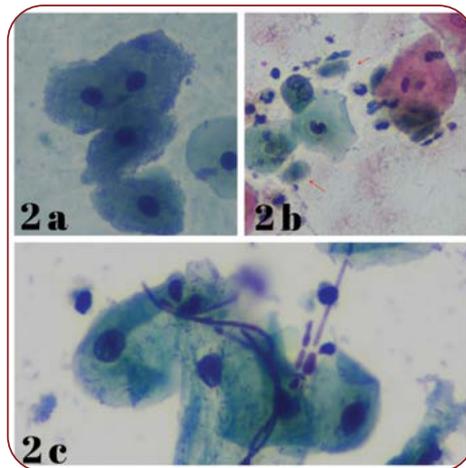


FIGURE 2. Pap smear, conventional type, 40X: (a) bacterial vaginosis with clue cells; (b) Trophozoites of *Trichomonas vaginalis*, marked by arrows; (c) pseudo hyphae of fungal organisms, morphologically resembling *Candida*.

commonest finding followed by *Trichomonas* and *Candida* (Figure 2 a, b, c, Table 1).

Cyto-histopathological correlation

Cyto-histopathological correlations were done in 65 cases, including 18 cases of ASCUS, four cases

TABLE 1. Spectrum of cervical cytology

NILM	1982	86.51%
ASCUS	26	1.13%
LSIL	4	0.18%
HSIL	9	0.39%
ASC-H	9	0.39%
SCC	7	0.31%
Adenocarcinoma	2	0.09%
AGUS	4	0.17%
Unsatisfactory	181	7.9%
Inflammation	59	2.58%
Atrophic	8	0.35%
Total	2291	100%

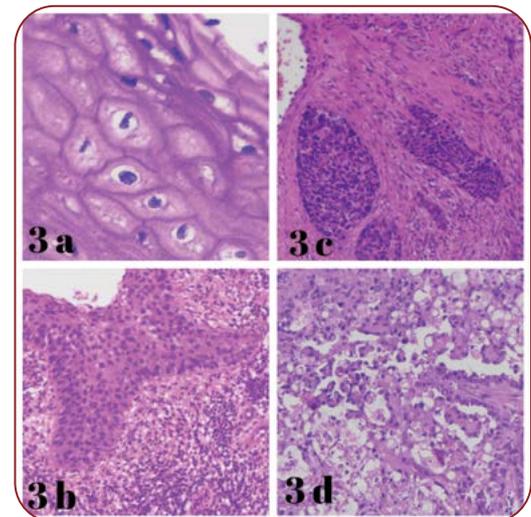


FIGURE 3. (a) LSIL, H&E stain-40X; (b) HSIL, dense mixed subepithelial inflammation, H&E stain-10X; (c) invasive SCC, H&E stain, 10X; (d) adenocarcinoma cervix, H&E stain, 10X.

of LSIL, nine cases of ASC-H, nine cases of HSIL, seven cases of SCC and two cases of adenocarcinoma. Biopsy was also performed in 16 patients with normal Pap smear who gave their consent. Out of 18 ASCUS cases, five (27.78%) showed negative results, five (27.78%) had CIN 1, three (16.78%) CIN 2/3 (Figure 3 a, b) and five (27.78%) cases had chronic cervicitis. Out of four cases of LSIL, negative results were seen in one case (25%) and chronic cervicitis in two (50%) cases. No cases of CIN 1 were detected (0%), and CIN 2/3 was found in one case (25%). Biopsy was done in nine cases of ASC-H. Normal results were seen in one

TABLE 2. Cyto-histopathological correlation

Cytology	Normal	Chronic cervicitis	LSIL (CIN 1)	HSIL (CIN 2+)	Malignancy	Total
Normal	7	9	0	0	0	16
ASCUS	5	5	5	3	0	18
ASC-H	1	1	1	5	1	9
LSIL	1	2	0	1	0	4
HSIL	1	0	0	5	3	9
Malignancy	0	0	0	0	9	9
Total	15	17	6	14	13	65

(11.11%) case, chronic cervicitis in one (11.11%) case, CIN 1 in one (11.11%) case, CIN 2+ in five (55.56%) cases and invasive squamous cell carcinoma in one (11.11%) case. Out of the nine cases of HSIL, normal results were found in one (11.11%) case, while CIN 1 was not detected in any of the examined samples; CIN 2/3 was seen in five (55.55%) patients and invasive carcinoma in three (33.33%) patients. Squamous cell carcinoma and adenocarcinoma were seen in seven (100%) subjects and adenocarcinoma in two (100%) cases (Figure 3 c, d, and Table 2).

In our institutional study, the specificity was 81.58% and sensitivity 83.33%. The correlation between cytology and histopathology was found to be 68.18%. The highest correlation was found in the HSIL category (88.89%). □

DISCUSSION

Cervical cancer screening had an important role in reducing the incidence of invasive cervical cancers. The present study aimed to find out the spectrum of cervical cytology and its correlation with clinical and histopathological diagnosis. Bethesda system 2014 was used to classify cytological findings. The results of our study were compared with those from various national and international studies. Carcinoma cervix is the leading cause of death from cancer among women. Pap smear is a simple and easy test used for the screening of this widely prevalent cancer. To confirm the sensitivity and specificity of the Bethesda classification, the cytological findings were correlated with histopathology considering it as a gold standard procedure.

Our study provides an analysis of age distribution, the various pattern of Pap smear, common

symptoms and facilitates cytological and histopathological correlation.

In our study, the majority of patients were aged between 21–70 years old, with 45.61% of all subjects being in the age group of 31–45 years. Participants' mean age was 41 years. The results of our study correlated with those reported by Sharma *et al* (4). Our study also suggests that most of the participants were sexually active.

In our study, almost 60% of cases were symptomatic and the commonest symptom was the white discharge, followed by vagina, pain in the lower abdomen, intermenstrual bleeding and dyspareunia, which is in agreement with the study done by Bamanikar *et al* in 2016 (1).

In the present study, out of the 2291 smears, 181 smears were reported unsatisfactory for evaluation. A total of 1982 (86.51%) patients were negative for intraepithelial lesion and malignancy and 61 had ECA (2.66%). In abnormal smear, 26 (42.62%) were ASC-US, nine (14.75%) were ASC-H, four cases (6.56%) were LSIL, nine (14.75%) were HSIL, seven (11.48%) were invasive squamous cell carcinoma, two (3.28%) cases reported as adenocarcinoma. Atypical glandular cells of undetermined significance (AGUS) were reported in four (6.56%) cases.

Among the inflammation categories, bacterial vaginosis was the commonest finding, followed by Trichomonas and Candida.

In our study, ECA rate was lower than the findings reported by other studies in the literature such as those conducted by Bamanikar *et al* (5.99%) (1) and Balaha *et al* (4.95%) (5). In our study, ASCUS was the most common finding in the ECA group (1.13%), which was comparable with other studies in the literature, including Kapila *et al* (6), Sharma *et al* (4) and Ouh *et al* (7).

In Sharma *et al*'s study, ASCUS was also a common finding (2.98%).

In our study, LSIL was seen in four (0.18%) cases and HSIL in nine (0.39%) cases, while Sharma *et al* (4) found those lesions in 1.19% and 0.66% of cases, respectively, and Abdulla *et al* (8) in 1% and 0.55% of cases, respectively.

Frank malignancy such as SCC & adenocarcinoma was detected among 0.39% of all participants in our study, while Sharma *et al* (4) and Tamboli *et al* (9) found it in 0.95% and 0.7% of their participants, respectively.

In the present study, the specificity was 81.58% and sensitivity 83.33%. The cyto-histopathology correlation was found to be 68.18%. The highest correlation was seen in the HSIL category (88.89%). These results were comparable with those reported by previously published studies (1, 4, 9, 10).

The Pap smear test was found to be equally sensitive to histopathological examination in detecting different cervical lesions early. However, for the confirmation of diagnosis it is advised to perform a biopsy if any abnormalities are detected in Pap smear for correlation. □

CONCLUSIONS

A range of new techniques has emerged in the diagnosis of various lesion of the cervix but, as these techniques are costly, they cannot be implemented in poor set up countries. In the present scenario, the Pap smear test is considered an ideal screening method for cervical car-

cinoma. A biopsy is always considered to be the gold standard for carcinoma cervix provided that it is taken from representative areas. The present study provides a positive cyto-histopathological correlation, especially for high-grade lesions. The collection of adequate materials and correct interpretation of abnormal cells is believed to ensure the success of screening for cervical cancer. □

Conflicts of interest: none declared.

Financial support: none declared.

Ethical approval: The present study was approved by the Institutional Ethics Committee.

MAIN POINTS

1. A range of new techniques has emerged in the diagnosis of various lesion of the cervix but, as these techniques are costly, they cannot be implemented in poor set up countries.
2. In the present scenario, the Pap smear test is considered an ideal screening method for cervical carcinoma.
3. The collection of adequate materials and correct interpretation of abnormal cells is believed to ensure the success of screening for cervical cancer.
4. Awareness, motivational programs, along with the use of liquid-based cytology (LBC) technique to reduce inadequate sampling errors, are recommended.

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