

Trends in cervical cytology of conventional Papanicolaou smears according to revised Bethesda System: A Study of 638 Cases

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ABSTRACT

Background: Cervical cancer remains an important health problem worldwide and more in developing nations. Cervical epithelial cell abnormalities in the Papanicolaou (Pap) smear represent a spectrum of cellular abnormalities that lie along the pathway, from in-situ lesions to invasive cancer.

Aim: To highlight the role of conventional Pap smear in detection of various cervical lesions to determine the prevalence of each and to correlate them with clinical profile.

Methods: A retrospective study comprising 638 conventional cervical Papanicolaou smears submitted to the department of Cytopathology. After fixation and staining, each smear was examined by at least two cytopathologists and the findings were recorded and classified according to the 2001 Bethesda System of reporting Pap smear cytology.

Results: Epithelial cell abnormalities were found in 13 smears of which Atypical squamous cells of undetermined significance (ASCUS) was seen in 10 (1.6%), High grade squamous intraepithelial lesion (HSIL) in 01 and Adenocarcinoma (Extrauterine) in 01 case. The Negative for Intraepithelial Lesion or Malignancy (NILM) category had 618 cases with reactive cellular changes associated with Non specific inflammation in 580 cases (90.9%). Specific inflammation was seen as candidiasis in 18 cases (2.8%), Trichomoniasis in 4 (0.6%), and Herpes simplex virus infection in 1 case.

Conclusion: Premalignant and malignant lesions of cervix are common and can be diagnosed early by conventional Pap smears. Conventional Pap smears are required not only for the diagnosis and management of the malignant lesions but it is also helpful in identifying the infectious etiologies and treatment in developing countries.

Keywords: papanicolaou smear, cervical intraepithelial neoplasia, carcinoma cervix

INTRODUCTION

Cervical cancer is one of the most common malignancies of women in India. Standardization of the Papanicolaou smear reporting by the use of the revised Bethesda System has unified various overlapping terminologies and has included specific statements regarding specimen adequacy, general categorization, interpretation, and results.¹ Globally, of all cancers in females 15% is attributed to carcinoma cervix, while in Southeast Asia, cancer cervix accounts for 20%-30% of all cancers and in Nepal 85% of all gynaecological malignancies.² The benefits of cytological screening have been established since last three decades; it is (cancer cervix) preventable by interception at preinvasive

stage, yet there are an estimated 132,000 new cases and 74,000 death occurring every year in India.^{2,3} National Cancer Registry of India (2007) 90,708 new cases of Carcinoma cervix with five-year survival rate of about 48%.⁴ Globally, 500,000 new cases are diagnosed annually and 280,000 women die of the disease.⁵ It is estimated that in India 1,26,000 new cases occur every year.⁶

Since the introduction of Pap test, a dramatic reduction has been observed in the incidence and mortality of invasive cervical cancer worldwide.⁷ The role of the Pap smear as a cancer screening tool for the cervix has been substantiated by several studies and has witnessed a decline in incidence and mortality

in developed world.⁸⁻¹¹

Hence, we undertook the present study using the revised Bethesda System (2001), to find out the prevalence and to carry out a clinicopathological and demographical analysis to establish the pattern of various cervical lesions in our population.

MATERIAL AND METHODS

Data of all conventional Pap smear cases (during Sep'2011 to Oct'2012) was retrieved and classified according to the 2001 Bethesda System of reporting Pap smear cytology. Six hundred seventynine requisitions for Pap smear was available in the catalogue section of department. However, complete set of information were available in 638 cases only which were further investigated. The detailed findings, copy of signed out reports, slides and clinical data of these patients were recorded. The smears were prepared from the patients presenting to the gynecologist, either for routine screening or with complaints like vaginal discharge, post-coital bleeding, intermenstrual bleeding, dyspareunia and lower abdominal pain. Relevant history of illness was obtained from the patient record. The submitted slides were prepared and labeled following the standard procedures. These prepared smears were then stained according to Papanicolaou's technique. The cytological interpretation of the smears was made according to the 2001 Bethesda system. The data was collected from the requisition form, reporting form and signed out report. Each set of slides for every patient had been evaluated by at least two cytopathologist as per convention in our hospital.

RESULT

The mean age of patients was 41.3 years. Maximum number of patients (250) was in the sexually active age group of 31-40 years (fourth decade). The most common presenting complaint was discharge per vaginum seen in 70% of the cases followed by lower abdominal pain/backache, bleeding per vaginum, dyspareunia, post-coital & post menopausal bleeding etc. Of the 638 cases analyzed, 13 were positive for epithelial cell abnormalities while 618 were negative for intraepithelial lesions. Diagnosis of atypical squamous cells of undetermined significance (ASCUS) was made in 10 cases (Fig. 1), Atypical Squamous Cells – cannot exclude high grade squamous intraepithelial lesion (ASC-H) in one, High grade Squamous intraepithelial lesion (H-SIL) in 1 and Adenocarcinoma (extrauterine), in a follow up patient of carcinoma ovary (Fig. 2).

Fig.1. ASC-US: Smears show squamous cells with slight nuclear enlargement, hyperchromasia, and cytoplasmic changes (Pap, X400).

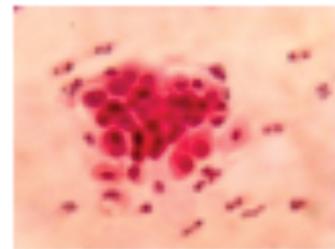
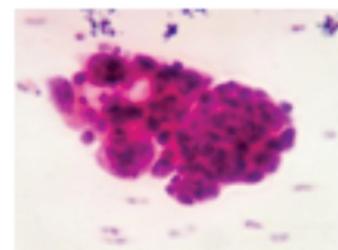


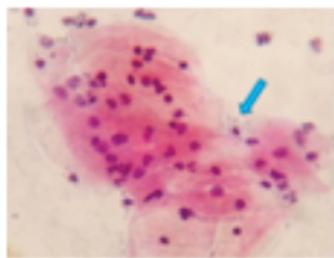
Fig.2. Adenocarcinoma (Extrauterine), Cluster of cells with enlarged, variably-sized hyperchromatic nuclei with prominent nucleoli. Smear background is clean (PAP, X400)



618 cases were reported as Negative for Intraepithelial Lesion or malignancy (NILM), 12

with in normal limits and 606 inflammatory of which nonspecific inflammation with reactive cellular changes were seen in 580 cases (90.9%). One of the smears showed radiation induced changes in a follow up case of Carcinoma Endometrium. Specific infectious agents were detected in 23 cases (3.6%); Candidiasis 18 cases (Fig. 3), Trichomoniasis 4 cases, and Herpes simplex virus infection 1 case - Table 1.

Fig.3. NILM, Inflammatory: Small, uniform, round budding yeast. Fungal organisms morphologically consistent with *Candida* spp.(*Torulopsis Glabrata*) (Pap X400).



The average age of patients for all the epithelial abnormalities was 45 years and most (76.8%) of the epithelial abnormalities were found in the age group 31-50 years of age (Table 2). Vaginal discharge was seen in 7 out of 13 patients of epithelial cell abnormalities.

Table 1: Categorisation of all cervical lesions

Cytological diagnosis	No of patients	Percentage (%)
NILM	618	96.8
Normal	12	1.8
Inflammatory	606	94.9
Non Specific	580	90.9
Candida	18	2.8
TV	04	0.6
HSV	01	0.1
Atrophic vaginitis	02	0.3
Radiation changes	01	0.1
Epithelial cell abnormalities	13	2.0
ASC-US	10	1.6
ASC-H	01	0.1
L-SIL	00	0.0
H-SIL	01	0.1
SCC	00	00
AGC	00	00
Adenocarcinoma NOS	01	0.1
Unsatisfactory	7	1.1
Total	638	100

Table 2: Epithelial cell abnormalities in all age groups

Age-group	ASC-US	ASC-H	L-SIL	H-SIL	SCC	Adeno carcinoma	%
<20	0	0	0	0	0	0	0
21-30	0	0	0	0	0	0	0
31-40	3	1	0	0	0	1	38.4
41-50	5	0	0	0	0	0	38.4
51-60	2	0	0	1	0	0	23.1
61-70	0	0	0	0	0	0	0
71-80	0	0	0	0	0	0	0
81-90	0	0	0	0	0	0	0
Total	10	1	0	1	0	1	100

Vaginal discharge and cervical erosion were the most common clinical presentations followed by suspicious cervix, hypertrophied cervix, unhealthy cervix, prolapse and cervical polyps. Colposcopy was abnormal in 16 cases and HPV DNA was suggested in 105 cases.

DISCUSSION

The 2001 Bethesda System maintains the “satisfactory for evaluation” and “unsatisfactory for evaluation” categories. Minimum cellularity requirements for a specimen to qualify as “satisfactory” differs depending on specimen type: an estimated 8000 to 12000 well-visualized squamous cells for conventional smears and 5000 squamous cells for liquid-based preparations. Specimens with more than 75% of epithelial cells obscured are “unsatisfactory.”¹ The previous category “within normal limits” and “benign cellular changes” has been combined into a single category “negative for intraepithelial lesion or malignancy.” In this way, reactive changes are more clearly designated as “negative.” “Other” has been added as a category for cases in which there are no morphological abnormalities in the cells per se; however, the findings may indicate some increased risk. These categories are mutually exclusive; therefore, if several findings are present, the general categorization is based on the most clinically significant result (e.g., epithelial cell abnormality).¹

Cervical cancer is the second most common cancer of women in the world comprising of approximately 12% of all cancers, while it is the leading cancer of women in the developing countries. The incidence of cervical cancer has decreased more than 50% in the past 30 years because of widespread screening with cervical cytology.² Cancer cervix is considered to be an ideal gynaecological malignancy for screening as it meets both tests and disease criteria for screening. It has a long latent phase during which it can be detected as identifiable and treatable premalignant lesions which precede the invasive disease and the benefit of conducting screening for carcinoma cervix exceeds the cost involved.^{3,12}

In the present study, 638 cases were analyzed, all of whom were married and mean age of the patients was 41.3 years which corresponds with the another study where the mean age was 37 years.² Thirteen cases of epithelial cell abnormalities were detected in our study which corroborates with various studies conducted at USA (2.3% to 6.6%), Middle East (1.6% to 7.9%) & Nepal (1.7%).^{2,13} ASCUS was more common in our patients however the incidence of ASCUS in Nepal and Saudi Arabia was less.^{2,14} Afrakhteh et al., found mean age of patients with LSIL, HSIL and invasive cancer to be 37.7, 41.7 and 54.5 years, respectively.⁷ Although we have not detected L-SIL but Elhakeem et al.¹³ recorded a progressive increase in development of LSIL to invasive carcinoma with increasing age. Sherwani et al., found LSIL and HSIL on cytology to be more prevalent in patients who started sexual activity before 20 years of age.¹⁴ The age of the only patient with HSIL was 52 years in our study with the prevalence being 0.1% however a high

prevalence rate of 3.7% was detected in Zimbabwe and China.^{15,16} In the study conducted by Bal et al., out of 273 cases of NILM, 74.3% were inflammatory, 8 were of Gardnerella, only one of Tricomonas & rest were non specific. Surprisingly no candidiasis case was recorded while we had seen 18 cases of candidiasis and 1 of Herpes Simplex virus infection.

Present study emphasized the significance of vaginal discharge and its association with neoplastic changes in the cervix. The results corresponded with many previous studies.¹⁷⁻¹⁹

The new term "ASC-H" is thought to include approximately 5% to 10% of Atypical Squamous cells cases overall.^{18,19} In our study the prevalence of ASCUS was 76.9%, HSIL accounted for 7.7%, Adenocarcinoma (Extrauterine) 7.7% of all cases of epithelial cell abnormalities. The results are comparable to those obtained by Patel et al. and Anuradha and Sinha.^{18,19} Few studies have documented a lower prevalence rate for SIL and invasive carcinoma.²⁰⁻²⁴ The reason for the overall low prevalence of abnormal epithelial lesions in this study might be due to small sample size. Two studies in Nepal also showed low prevalence due to the same reasons^{2,22} Many patients with abnormal Pap results had a healthy cervix. In our study 53 patients had normal cervix on visual inspection but most of them with abnormal Pap smears. This signifies that cervical cancer screening, based only on clinical impression and visual examination, is quite unpredictable in relation to cytological screening. This also connotes the value of universal cervical cancer screening, irrespective of the visual impression. Estimates suggest that 10% to 20% of women with ASC have underlying CIN 2 or 3 and that 1 in 1000 may have invasive cancer. LSIL is generally a

transient infection with HPV, while HSIL is more often associated with viral persistence and higher risk for progression.²⁴⁻²⁶

CONCLUSION

Cervical cancer continues to be the commonest cause of death among women in developing countries, largely due to the inability to sustain effective cytology-based screening programs. While this burden may come down following implementation of the human papilloma virus (HPV) vaccine, screening will still be required.

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