Cytohistopathological Study of Cervical Lesions

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Abstract

Introduction: Carcinoma of cervix is the third most common malignancy encountered among women globally. About 80% of these cases occur in the developing countries. With the effectiveness of the papanicolaou (PAP) cytologic test in the early detection of precancerous state and accessibility of cervix for a biopsy the mortality rate due to carcinoma of cervix has declined statistically. The present study was undertaken to correlate premalignant and malignant smears with histopathological findings observe the spectrum of lesions in cervical smears and the clinical findings in the same.

Materials and Methods: The cervical cytological smears and biopsies received incessantly in the Department of Pathology, SDMCMSH Dharwad over a period of 2 years were stained with the criterion PAP and hemotoxylin and Eosin stains respectively in the present analytical study.

Results: A total number of 5559 smears studied included inflammatory changes 4413 (79.38%), normal 983 (17.68%), precancerous and malignant 123 (2.2%), and inadequate 40 (0.7%). 123 smears showing atypical and malignancy included atypical squamous cells of undetermined significance (ASCUS) 59 (47.96%), atypical glandular cells of undetermined significance (AGUS) 7 (5.69%), low-grade squamous intraepithelial lesion (LSIL) 20 (16.2%), high-grade squamous intraepithelial lesion (HSIL) 15 (12.18%), positivity for malignant cells 5 (4%), squamous cell carcinoma 16 (13%), and adenocarcinoma 1 (0.8%). Biopsies showed 100% accuracy in malignant lesions. 3 (11.11%) of 27 biopsied cases of ASCUS and 4 (44.44%) of 9 biopsied cases of HSIL were malignant. In cases of AGUS and LSIL, all biopsies showed nonmalignant features.

Conclusion: PAP smear test is found to be a sensitive and highly effective method for the detection of cervical neoplastic changes.

Key words: Atypical squamous cells of undetermined significance, Cervix biopsy, High grade squamous intraepithelial lesion, Squamous cell carcinoma, PAP smear

INTRODUCTION

Cervical cancer is an important cause of morbidity and mortality among females worldwide. With the effective implementation of screening procedure, awareness program, education, improved quality of living incidence of carcinoma cervix has been drastically decreased in developed countries; however, it is still one of the common neoplasm in developing countries. In India, it is one of the most common neoplasms in females with an incidence of 14.42/1,00,000 population and mortality rate of 2.83/1,00,000 population.[1] The cervical epithelium presents a spectrum of cervical intraepithelial neoplasia (CIN) changes as precancerous state. Most cervical cancers can be detected at preinvasive state with an adequate cytological screening and treated appropriately thus preventing overt progression of the lesion to full blown cancer and in turn decreasing morbidity and mortality.[2] With the effectiveness of the papanicolaou (PAP) cytologic test in early detection of precancerous state and accessibility of cervical biopsy the mortality rate due to carcinoma cervix has declined statistically.

The present study was planned to study the usefulness of cervical cytology by PAP smear in detecting and classifying different non-neoplastic, pre-neoplastic, and neoplastic lesions of cervix and correlate the PAP smear cytology with histological findings.

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MATERIALS AND METHODS

It was a retrospective study which involved the study of cervical cytological smears and biopsies received in the department of pathology, SDMCMS&H, Dharwad over a period of 2 years. Ethical clearance was obtained from institutional ethical committee before the start of the study. Cervical smears were prepared by using disposable ayre's spatula, fixed in 95% alcohol and stained by conventional PAP technique and interpreted according to the guidelines of 2001 bethesda system. Total 5559 smears received were analyzed. For the histopathological correlation of preinvasive and invasive lesions corresponding cervical biopsy (punch biopsy and hysterectomy specimen) slides were collected and studied in detail. Clinical history of the same was obtained by studying clinical records.

RESULTS

A total number of 5559 smears were studied among them 5396 smears were diagnosed to be negative for intraepithelial lesion or malignancy, in that 4413 (79.38%) cases showed inflammatory changes which included 446 cases of reactive changes, 349 cases of fungal infection morphologically consistent with candida species, 298 cases of trichomonas inflammation and 2 cases of herpes simplex infection. There were 983 (17.68%) normal smears, precancerous, and malignant cases constituted 123 cases accounting to 2.2% cases of the study. There were 40 (0.7%) inadequate smears which could not be evaluated.

Smears showing abnormal findings like precursor lesions and frank malignancy were studied in detail which constituted 2.2% of all the cases. Clinical data of these were obtained from medical records. It was observed that the distribution of these lesions showed wide range of incidence from second to eighth decade (age group 27-82 years). Atypical squamous cells of undetermined significance (ASCUS) was seen in 59 (47.96%) cases which was more common among the age group 41-50 years, atypical glandular cells of undetermined significance (AGUS) seen in 7 (5.69%) cases and was more common in 41-50 years, low-grade squamous intraepithelial lesion (LSIL) seen in 20 (16.2%) cases and common in 3rd decade, high-grade squamous intraepithelial lesion (HSIL) in 15 (12.18%) cases common in 6th decade, positivity for malignant cells 5 (4%) cases, common in 5th decade, squamous cell carcinoma accounting to 16 (13%) cases, common in 51-60 years and adenocarcinoma 1 (0.8%) seen in a 80-year-old woman (age wise distribution Table 1).

Most common complaint with which these patients came was discharge per vagina, followed by intermenstrual spotting and irregular bleeding. There were very few PAP smears which came as a part of the routine screening process. All 123 cases were parous.

In 123 cases of abnormal smears corresponding cervical tissue biopsy was available in 62 cases (54.54%). Smears diagnosed to be malignant showed good correlation with histopathology. There were 16 cases of SCC diagnosed cytologically; biopsy correlation was available in 15 cases in that 13 (86.66%) were consistent (Figure 1), and 2 (13.33%) were adenocarcinoma. However, all 15 cases were malignant which was picked in PAP smear study. One case of adenocarcinoma diagnosed in PAP study correlated histopathologically (Figure 2).

Of 59 cases of ASCUS biopsy was available in 27 cases, 3 (11.11%) of 27 biopsied cases of ASCUS showed features of CIN and majority of the cases, i.e., 21 (77.78%) showed features of chronic cervicitis. In 14 cases of HSIL biopsy was available in 10 cases in which 2 showed features of microinvasive carcinoma, 3 cases showed features of CIN (Figure 3) and 4 cases showed features of chronic cervicitis. In cases of AGUS and LSIL, all biopsies showed nonmalignant features (Table 2 PAP smear biopsy correlation).

DISCUSSION

Prevalence of carcinoma cervix worldwide is 3,95,5000/year and mortality is 1,95,000/year.[2] Women under 45 years of age has 2% chance of developing cervical cancer.[3] However, screening programs have reduced the incidence and mortality from carcinoma cervix in developed countries. It is well accepted that PAP smear has been the most effective cancer screening test ever introduced. The screening test has achieved a reduction in the death rate of >70% for a prevalent cancer.[2]

The success of PAP test has resulted in unrealistic community expectations, with a consequent rise in litigation. It is important to be aware that as with any pathological tests, there are recognizable false results for PAP test. Traditionally, the gold standard for assessing the performance of PAP smears prediction has been the histology of cervical biopsies. Although it is acknowledged that histology also suffers certain drawbacks, since its lesser extent, it nevertheless, provides a reasonable parameter to gauge the performance of the PAP test.[4]

The age range of patients with epithelial cell abnormality, i.e., pre-neoplastic and neoplastic lesions was 24-82 years and constituted 2.2% cases of the study which can be

Table 1: Prevalence of abnormal cervical smears in different age groups

Diagnosis	21-30	31-40	41-50	51-60	61-70	71-80	81-90	N (%)
ASCUS	3	14	27	7	5	2	1	59 (47.96)
AGUS	-	2	3	2	-	-	-	7 (5.69)
LSIL	1	10	6	2	1	-	-	20 (16.2)
HSIL	1	3	7	2	1	1	-	14 (12.18)
SCC	-	3	2	7	4	-	-	16 (13)
Positive for malignancy	-	1	1	1	1	1	-	5 (4)
Adenocarcinoma	-	-	-	-	-	1	-	1 (0.8)
Total	5	33	46	21	12	5	1	123 (100)

ASCUS: Atypical squamous cells of undetermined significance, AGUS: Atypical glandular cells of undetermined significance, LSIL: Low grade squamous intraepithelial lesion, HSIL: High grade squamous intra epithelial lesion, SCC: Squamous cell carcinoma
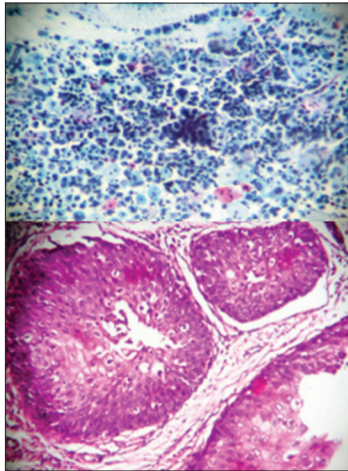
Figure 1: PAP and Biopsy - Squamous cell carcinoma
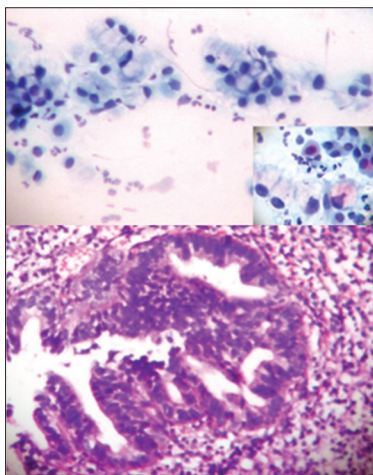

Figure 2: PAP and Biopsy Adenocarcinoma

Table 2: Correlation of PAP smear and cervical biopsy histopathology

Pap smear	Number of cases	Histopathology	Number of cases (%)
ASCUS	27	Chronic cervicitis	21 (77.78)
		Normal cervix	3 (11.11)
		CIN	3 (11.11)
AGUS	4	Chronic cervicitis	2 (50)
		Normal cervix	2 (50)
LSIL	5	Chronic cervicitis	2 (40)
		Normal cervix	1 (20)
		Decubitus ulcer	1 (20)
		Reparitive change	1 (20)
HSIL	10	Chronic cervivitis	4 (40)
		Normal cervix	1 (10)
		Micro INV CA	2 (20)
		CIN	3 (30)
SCC	15	SCC	13 (86.66)
		Adenocarcinoma	2 (13.34)
Adenocarcinoma	1	Adenocarcinoma	1 (100)

ASCUS: Atypical squamous cells of undetermined significance, AGUS: Atypical glandular cells of undetermined significance, LSIL: Low grade squamous intraepithelial lesion, HSIL: High grade squamous intra epithelial lesion, SCC: Squamous cell carcinoma, CIN: Cervical intraepithelial neoplasm
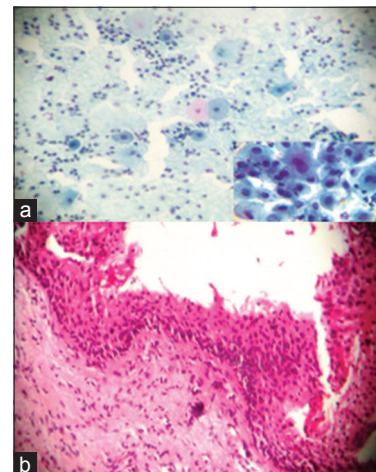
Figure 3: PAP – High grade squamous intraepithelial lesion Biopsy – Cervical intraepithelial neoplasia

compared to the study done by Tailor *et al.* wherein age range was 2nd to 8th decade and abnormal PAP smears accounted to 2.61% of total smears taken.[5]

ASCUS was the most common abnormal PAP smear finding noted which can be compared to the study by Tailor *et al.* and Patel *et al.*[6]

This study is done to evaluate the usefulness of PAP smears. 123 cases (neoplastic and pre-neoplastic lesions) were studied in detail; in 62 cases the cytologic diagnosis

was compared with the histopathologic diagnosis. The overall concordance rate in this study is 62.18% which can be compared to Saha *et al.* study with concordance rate of 60%.[7]

The concordance rate of SCC in this study is 86.66% were as Jain *et al.* study showed 83.6%.[8] The 2 discordant cases were found to be adenocarcinoma on biopsy. However, malignancy was picked in PAP smear evaluation itself which prompted for further management.

A total of 27 cases of ASCUS biopsied showed 3 cases of CIN (11.11%) thus stressing the importance of follow-up of the lesions. In the case of AGUS, all cases showed benign features.

All positive cases of malignancy in the smears studied were consistent with biopsy, showing the high sensitivity of PAP smears in detecting the lesions.

With the concordance rate of 62.18% in this study, it is concluded that PAP smears significantly correlate with biopsy. However, repeat smear at regular intervals, uniform reporting following the standard protocol (Bethesda 2001) should be done, and colposcopic guided biopsy should be encouraged to reduce false positive and false negative rates.

CONCLUSION

PAP smear test is found to be a sensitive and highly effective method for the detection of cervical neoplastic changes. Cytological features significantly correlate with histological findings. Thus, screening procedures should be implemented in early age in sexually active females to detect the lesion in an early stage.

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