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Lesions of uterine cervix by cytology and histopathology- A prospective study for a period of two years

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Abstract

Background: Carcinoma uterine cervix is one of the leading causes of cancer death among women worldwide. It is well known that cervical cancer morbidity and mortality could be significantly reduced with an active cervical smear screening (Pap smear) program.

Objectives: To study the cytology of various types of neoplastic and non-neoplastic lesions of cervix and to evaluate the accuracy of cervical smear study.

Materials and Method: Cervical smears were obtained with Ayer's spatula from patients presenting with history of discharge per vaginum, irregular bleeding, post coital bleeding, post-menopausal bleeding, pain abdomen and mass per vaginum to the Department of Obstetrics and Gynecology, SVS Medical College and Hospital, Mahabubnagar. Smears were fixed in alcohol immediately and stained by Papanicolaou stain and H & E stain. The abnormal smears were followed by cervix biopsy and cytology findings were correlated.

Results: In the present study, a total of 1000 cervical smears were studied and 235 out of 1000 cases were followed by histopathological study. Out of these 1000 cases, one hundred and seventy nine (17.9%) cases were neoplastic, seven hundred and six (70.6%) cases were inflammatory smears, ninety (9.0%) cases were normal study and twenty five (2.5%) cases were inadequate to evaluate. Among 179 neoplastic cases, eighteen (10.06%) were carcinomas, forty six (25.07%) were HSIL and one hundred and fifteen (64.24%) were LSIL. The sensitivity of cervical cytology was 88.06% and specificity was 95.24% in the present study.

Conclusion: Pap smear examination is widely accepted screening method. Countries like India with predominant rural population are having low socio-economic status, marriage at an early age and poor medical facility. Screening females by cervical smear helps to detect carcinoma cervix in its preinvasive phase. The procedure is easy, inexpensive and rapid.

Keywords: Papanicolaou Smear; Cytohistologic Correlation; Cervical Cytology.

Introduction

Cancer of the uterine cervix is an important cause of morbidity and mortality among women worldwide and a leading public health problem.(1) In India, cancer of the uterine cervix is the most frequent neoplasm among women, accounting for 20%-50% of all female cancers and 80% of all female genital cancers.(2) Approximately one out of every 142 women will be diagnosed with cervical cancer at some point in her life.(3) As the phases that precede the lesion in the natural progress of invasive cervical cancer can be easily discovered and treated, the disease is well suited to screening programs. The Papanicolaou test is an established method for examining the cells collected from the cervix to determine signs of pre-neoplastic differentiation. Also reactive and inflammatory conditions of cervix and vagina can be recognized.(4)

It has been known that the squamocolumnar junction of cervix is the site of predilection for carcinoma of the cervix. In an effort to study early malignant changes in the squamous cells thrown off specifically from this focus, the spatula cytology technique was developed and this is a means of collecting the cells before their exfoliation.(5) The efficacy of cervical smear study was established by George N. Papanicolaou in 1928.(2) Cytologic screening programs have led to a large decline in cervical cancer incidence and mortality in developed countries; whereas in developing countries the incidence is still high because of lack of resources for effective screening programmes.(6) With an increase in the incidence of HIV infection there is an increase in the incidence of HPV infection of cervix. HPV infection is a known precursor of pre-neoplastic and neoplastic lesions of the cervix. Hence, there is a need to study various neoplastic and non-neoplastic lesions of cervix by cervical smear study and correlate with histopathological findings when needed. This study aims at correlating the cytological diagnosis with the histopathological diagnosis.

Methodology

The present study was done to study the cytology of various types of neoplastic and non-neoplastic lesions of cervix and to evaluate the accuracy of cervical smear study. The study was conducted in the Department of Pathology, SVS Medical College, Mahabubnagar, Andhra Pradesh, from August 2009 to July 2011. Smears were obtained from patients attending the department of Obstetrics and Gynecology, SVS Medical College and Hospital, Mahabubnagar, presenting with complaints of discharge per vaginum, irregular menstrual cycles, post-menopausal bleeding, pain abdomen and mass per vagina and sent to the Department of Pathology, SVS Medical College, Mahabubnagar. Detailed clinical data was obtained and noted on a structured proforma. Patients attending Obstetrics and Gynecology OPD with

complaints of white discharge, pain abdomen, irregular bleeding, mass per vaginum and post-menopausal bleeding were included in the present study. Antenatal, post-partum cases were excluded.

Methods of Reporting:

a. Cytology: The Bethesda System (TBS)2001
b. Histopathology: WHO classification

Out of 1000 cases studied cytologically, biopsies were available for 235 cases (150 cervical punch biopsies and 85 hysterectomies). Correlation was done for 235 cases.

Cervical smear was taken by the Gynecologist after obtaining consent of the patient. Cervix of the patient was exposed adequately with a speculum. The squamocolumnar junction was visualized, with the hooked end of Ayer's spatula, squamocolumnar junction was scraped gently throughout its circumference and material was transferred to glass slides. Two such smears were fixed with 95% alcohol immediately and stained by Papanicolaou stain and H & E stain. The abnormal smears showing preneoplastic and neoplastic changes were followed by cervical biopsy.

Cervical biopsy procedure was done by the Gynecologist and the specimen was sent to the Department of Pathology. After explaining the procedure and obtaining the consent of the patient, cervical cone biopsy was taken. The anterior lip was grasped with a volselum applied well above the area to be excised for biopsy. The squamocolumnar junction was visualized. A circular incision was made with a sharp pointed thin bladed knife around and well outside the suspected area. Incision was then deepened with circular sweeps until the region of the internal os was reached. After removal of the tissue, hemostasis was achieved and then cavity was closed by a double suture. The excised tissue thus obtained was fixed in 10% formalin, processed and embedded in paraffin blocks; 5-6 µ thick sections were cut and stained with haematoxylin and eosin. The histopathological findings were evaluated and correlated with cervical cytology findings. Statistical data pertaining to sensitivity, specificity and efficacy rate of cervical cytology were calculated.

Results

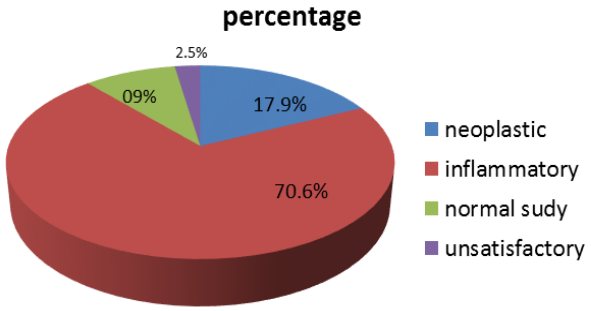

Fig. 1: Cytologic diagnosis in 1000 smears

The prevalence of neoplasia was 17.9%. Inflammatory lesion was 70.6%, Normal study was 9 % and percentage of inadequate smears was 2.5%. Age of patients ranged from 18 to 80 years. The mean age was 39 years.

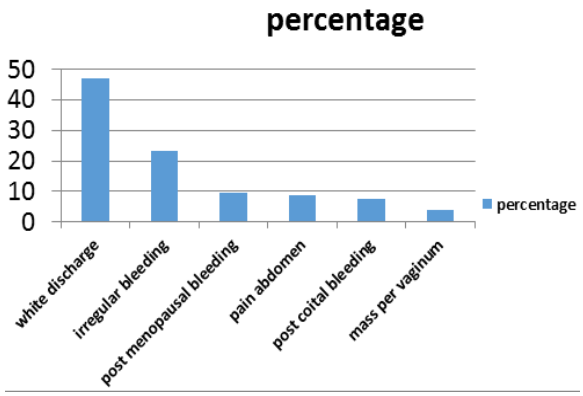

Fig. 2: Various clinical presentations in the present study

The major presenting complaint was white discharge per vaginum seen in 469 patients (46.9%). Followed by irregular bleeding, forming 23.3% and only 40 patients (4%) presented with mass per vaginum.

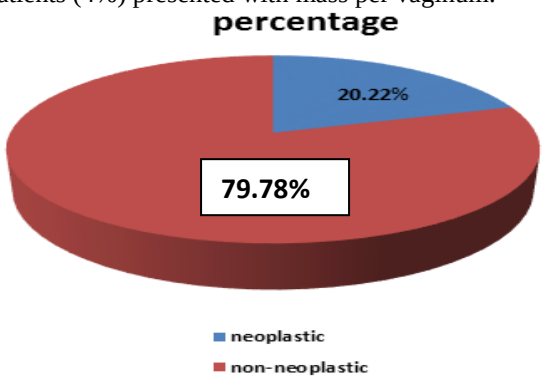

Fig. 3: Types of cervical disease based on cytological study

Out of 885 cases, 179 (20.22%) were neoplastic lesions. The ratio of neoplastic to non-neoplastic lesions was 1:4.

Table 1: Distribution of neoplastic lesions

Lesion	Number of cases	Percentage
Malignant	18	10.06
Pre-malignant	161	89.94
a. HSIL	46	25.7
b. LSIL	115	64.24
Total	179	100

Ratio of premalignant to malignant lesions was 8.9:1. In the premalignant lesions, HSIL constituted 25.70% and LSIL to 64.24%.

Table 2: Percentage distribution of non-neoplastic lesions on cytology

Lesion		Number of cases	Percentage
Reactive cellular changes		652	92.35
	Non-specific inflammation	645	91.35
	Atrophic vaginitis	7	1
Infections		54	7.65
	Trichomonas	18	2.55
	Herpes simplex virus	05	0.71
	Candida	14	1.98
	Bacterial vaginoses	17	2.41
Total		706	100

Maximum number of cases was diagnosed as nonspecific inflammatory changes. The percentage of specific infections accounted for 7.65% of cases. Among specific infections, maximum were 18 (2.55%) cases of Trichomonas. In this study, 235 cases were studied histopathologically for which cervical smear diagnoses were available.

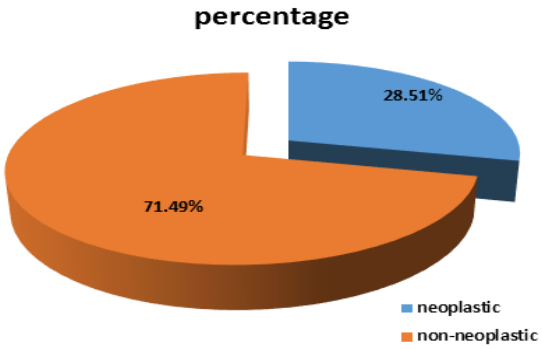

Fig. 4: Histopathologic diagnosis in 235 cases

Out of 235 cases studied histologically, 67 (28.51%) were neoplastic and 168 (71.49%) were non-neoplastic.

Table 3: Distribution of neoplasia on histopathology

Lesion		Number of cases	Percentage
Malignant		18	26.87
	Squamous cell carcinoma	18	26.87
	Adenocarcinoma	00	00
Pre-malignant		49	73.13
	HSIL	37	55.22
	LSIL	12	17.91
Total		67	100

The prevalence of malignant lesion was 26.87% and premalignant lesion 73.13%. There were 18 (26.87%) cases of Squamous cell carcinomas. There were 12(17.91%) cases of LSIL and 37 (55.22%) cases of HSIL.

Table 4: Various non neoplastic lesions on histopathology

Diagnosis	Number of cases	Percentage
Non specific cervicitis	131	77.98
Polypoidal endocervicitis	25	14.88
Microglandular hyperplasia	10	5.95
Tuberculosis	2	1.19
Total	168	100

Maximum number of cases was diagnosed as chronic nonspecific cervicitis i.e. 131 (77.98%) followed by 25 (14.88%) cases of polypoidal endocervicitis.

Table 5: Diagnostic accuracy of cytology in neoplastic lesions

Histopathology diagnosis	Number of cases	Cytology diagnosis	Number of cases	Diagnostic accuracy
Squamous cell carcinoma	18	Squamous cell carcinoma	18	100%
HSIL	37	HSIL	31	83.78
LSIL	12	LSIL	10	83.34

In this study, 8 cases had false negative diagnosis on cytology giving a false negative rate of 11.94%. 8 cases were diagnosed as premalignant lesions (LSIL + HSIL) on cytology, but on histopathology they were diagnosed as chronic cervicitis giving a false positive rate of 4.76%.

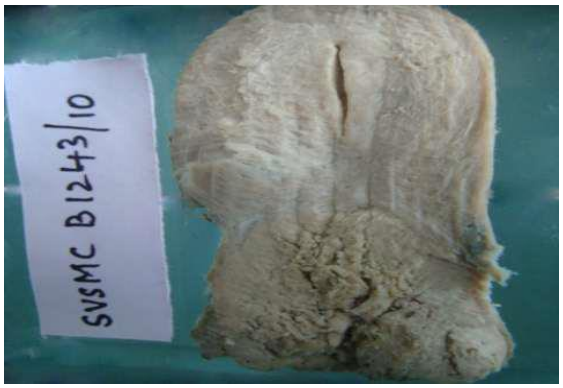

Fig. 5: Hysterectomy specimen showing growth in the cervix

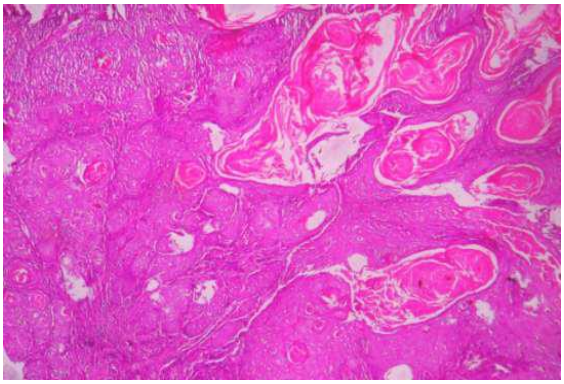

Fig. 6: Squamous cell carcinoma: Showing malignant cells infiltrating the stroma

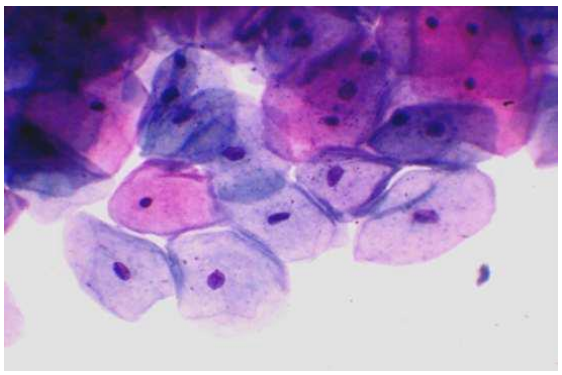

Fig. 7: LSIL: Showing koilocytic change (Pap, 10x40)

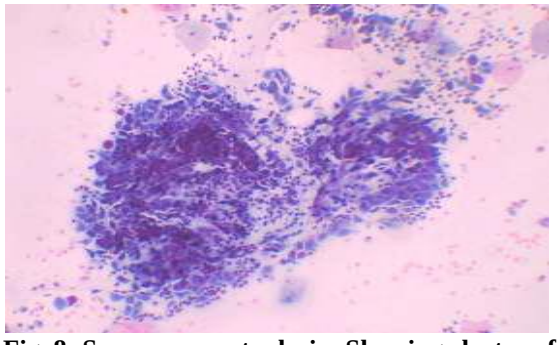

Fig. 8: Squamous metaplasia: Showing cluster of cells with cytoplasmic projections

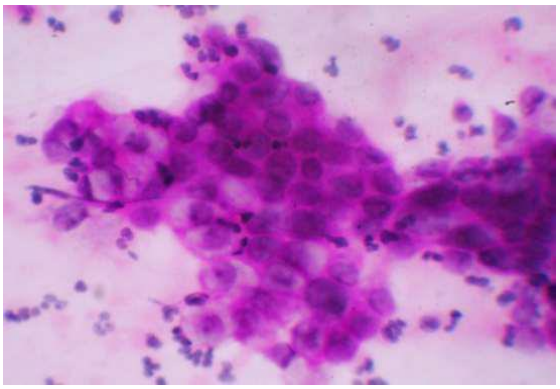

Fig. 9: Reactive change: Showing sheet of reactive endocervical cells with prominent nucleoli

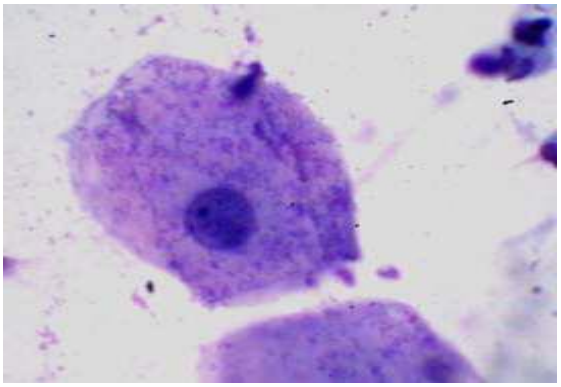

Fig. 10: Bacterial Vaginosis

Discussion

The cytologic diagnosis of cervical smears has become a very important screening test for the detection of pre-invasive and invasive cervical epithelial abnormalities. Screening of female population for cervical neoplasia is a simple, inexpensive and reliable method which greatly reduces the mortality and morbidity associated with carcinoma cervix, if detected in its pre-invasive stage. The present study was conducted to know the accuracy of cervical cytology in diagnosis of cervical neoplasia. An attempt has been made to compare the various risk factors and parameters in the study with the results obtained by different workers.

1000 cases including neoplastic and non-neoplastic lesions were studied and in 235 cases the cytologic diagnosis was compared with the histopathologic diagnosis. The mean age in the present study was 39 years which was comparable to the study of Gupta et al.[7] in which the mean age was 39.4 years. The mean age was slightly higher in other studies as reported by Mostafa M et al[8] (41.66 years) and Autier P et al[9] (46 years), lower in study reported by Nazan et al[10] (38 years). All these studies indicate that carcinoma cervix is common in elderly age group.

All the studies showed increase in the ratio indicating the higher rate of neoplastic lesions in developing countries as compared to developed

countries. Mulay et al[11] found 44 out of 6010 (0.73%) inadequate smears and Misra et al[12] observed that 2956 (8.1%) out of 36484 smears were inadequate, whereas in the present study we found 25 out of 1000 (2.5%) inadequate smears. Similar to other studies, scanty number of cells, admixture with blood or dense inflammation were responsible for inadequacy in the present study also.

In the present study, the ratio of premalignant to malignant lesions was 8.9:1, which was comparable to study of Misra et al,[12] where the ratio was 11:1. However, the rate of premalignant lesions was much higher as reported by Yeoh et al[13] with ratio of 45.2:1. Sherwani et al[14] had found a lower rate of premalignant lesions, the ratio being 3:1 respectively.

The percentage of LSIL and HSIL was 64.24% and 25.70% respectively in the present study and similar findings were reported by Sherwani RK et al,[14] where LSIL was 71.11% and HSIL was 15.56%. However, Mulay et al[11] and Mostafa et al[8] have reported a higher percentage of HSIL compared to LSIL. This probably indicates variation in individual interpretation of SIL. As with the other studies, the percentage of carcinoma was lower than the percentage of dysplasia in the present study. Mean age for premalignant lesions was 37.71 years in the present study. Misra et al[12] found maximum frequency of SIL (10.71%) in older women beyond 40 years of age, indicating increased incidence of premalignant lesions in elderly females. Sherwani RK et al[14] found 27 (64.4%) cases of LSIL and HSIL in 3rd and 4th decades.

Average age of carcinoma cervix in the present study was found to be 45.94 years which was similar to that reported by Jamal et al[15] where it was 45 years.

Specific infections accounted for a very small percentage (7.65%) of cases in the present study as compared to the study of Malik et al.[16] The percentage of specific infections was 8% in their study and was mainly due to Coccobacilli causing shift in vaginal flora. The common infective organism found in the present study was Trichomonas (2.55%) followed by Candida (1.98%). The majority of inflammatory cases were due to non-specific inflammation and squamous metaplasia in the present study. Similar findings were reported by Malik et al.[16]

The major presenting complaint was white discharge per vagina in the study of Sherwani RK et al[14] (42.5%). In the present study, majority of the patients complained of white discharge per vagina (46.9%), the other symptoms being irregular bleeding (23.3%), post-menopausal bleeding (9.7%), pain abdomen (8.7%) and post coital bleeding (7.4%). Misra et al[12] reported vaginal discharge and post coital bleeding as common complaints in women with dysplasia. In the present study also, vaginal discharge was the common complaint in women with dysplasia. Chief complaints in carcinoma cervix was post-menopausal bleeding as reported by Sherwani RK et al[14] and Misra et al.[12] In the present study, 6 cases presented with discharge per vaginum, 5 cases presented with irregular bleeding, 4 cases with post coital bleeding and 3 cases presented with post-menopausal bleeding.

In the present study, maximum cases of SIL (49.06%) and SCC (88.88%) had 3 or more than 3 children. Similar findings were noted in studies by Misra et al,[12] Sherwani RK et al[14] and Shankarnarayana et al.[17]

The diagnostic accuracy of cytology for the diagnosis of carcinoma was 100% in the study of Sherwani et al[14] and the present study. Mostafa et al[8] (68%) and Yoeh et al[13] (54.5%) found a lower accuracy rate which could be attributed to under-diagnosis or due to errors in interpretation.

In the present study, the diagnostic accuracy for HSIL was 83.78%. 31 cases were diagnosed correctly as HSIL on cytology. In 6 cases, the atypical cells were not found in the smear due to sampling error. Yoeh et al[13] found a diagnostic accuracy rate of 55.56%. 72 out of 128 cases were accurately diagnosed on cytology. Ten each were diagnosed as inflammatory and ASCUS, thirty two as LSIL and 4 were over diagnosed as Squamous cell carcinoma. This could be attributed to either under diagnosis or sampling error. Mostafa et al[8] also reported similar findings in their study.

The diagnostic accuracy for LSIL was 50.7% in the study of Yoeh et al.[13] 37 of 86 were diagnosed accurately on cytology. 19 cases were over diagnosed as HSIL. Eleven cases were diagnosed as ASCUS and nineteen as inflammatory smears. Mostafa et al[8] detected an accuracy rate of 77.7% and was mainly due to overestimation by cytology in twelve cases (11 HSIL and 1 carcinoma). However, the present study noted the accuracy rate of 83.34% for LSIL. The overall accuracy of cervical cytology was found to be 88.06% in the present study. Yeoh et al[13] found a lower rate of 52%. Under diagnosis by cytology was an important reason for inaccurate diagnosis. Under diagnosis by cytology was noted in 11.94% of cases in the present study. The rate was lower than described by Mostafa et al[8] (27%). Over-diagnosis by cytology was detected in 4.76% of cases in the present study. However, Mostafa et al[8] noted a higher rate of 26%. So both under-diagnosis and over-diagnosis were responsible for inaccurate diagnosis. No case of adeno-carcinoma was found in the present study. Mostafa et al[8] reported 41 cases (5.6%) of adeno-carcinoma. The cervical cancer screening for adeno-carcinoma was less effective because of sampling difficulties. According to the study of Malik et al[16] the most common biopsy diagnosis was cervicitis, 29 (31.5%), followed by immature squamous metaplasia, fifteen (16.3%) and reserve cell hyperplasia, ten (10.8%). In the present study, the most common finding on histopathology was nonspecific cervicitis, 131 (77.89%) followed by polypoidal endocervicitis, 25 (14.88%). In the present study, 18 cases were diagnosed as Trichomonas vaginalis infection on cytology.

However, Trichomonas were not seen on histopathologic sections which showed chronic nonspecific cervicitis. This indicates that cervical cytology is more sensitive than histopathology in diagnosing Trichomonas infection. We described two cases of tuberculous cervicitis on histopathology. However, there was no evidence of granulomas, macrophages or caseous necrosis on cytology. Similarly, smear from the patient with histologically diagnosed micro-glandular hyperplasia showed no evidence of such findings on cytology. This could be attributed to difficulty in sampling.

In the study of Wilkinson[18] 60% of false negative smears were due to sampling errors and screening errors accounted for approximately 40% of false negative errors. Interpretation errors were rare. In the present study, sampling errors accounted for most of the false negative smears.

Conclusion

The regular screening of population by Pap smear is a cost-effective method for early detection of premalignant and malignant cervical lesions and down staging of carcinoma cervix. The procedure is simple, inexpensive and can be performed in the outpatient department. Hence, it should be recommended routinely as a method of improving reproductive health.

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