

Original Research Article

## Cytodiagnostic Study of Cervical Lesions Using the Bethesda System with Histopathological Correlation

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### ABSTRACT

**Background:** The histogenesis and progression of cervical carcinoma is well documented. It is possible to prevent the development of invasive carcinoma by identifying and treating pre invasive lesions. The objectives of the study were to study the usefulness of cytology in detecting various cervical lesions, to evaluate and interpret the cases of epithelial lesions according to The Bethesda 2001 classification System and to correlate cytology diagnosis with histopathology diagnosis. The sensitivity, specificity and positive predictive value of Pap smears were calculated and compared.

**Materials and Methods:** The study was performed on 100 cases on women between the age group of 18 to 70 years, presenting with complaints of white discharge per vaginum, pain abdomen and menstrual irregularities. Pap smears were obtained and stained with Papanicolaou stain. The conventional Pap smears were interpreted according to The Bethesda System 2001.

**Results:** The median age was 34 years (range 18-70). The cytological evaluation of 100 Pap smears revealed majority of cases (52%) as benign/inflammatory lesions, NILM (15%), organisms (10%) and neoplastic lesions (23%). On histopathological evaluation, 85 cases were reported as non neoplastic lesions and 15 cases as neoplastic ones. The overall concordance rate was 76.1% and discordant cases were 23.8%. The sensitivity of cytology in detecting cervical lesions was 71.4% and specificity was 89.8%.

**Conclusion:** The Pap smear has good sensitivity and specificity and positive predictive value in detecting high grade lesions and malignancy. The discrepancy can be minimized by following The Bethesda system for adequacy of sampling.

**Keywords:** The Bethesda system, Pap smears, NILM, Squamous intraepithelial lesions, Squamous cell carcinoma.

### INTRODUCTION

Cancer of the uterine cervix is a global health problem. It comprises approximately 12% of all cancers among women globally. According to a recent data, an estimated 4,70,600 new cases of cervical cancer occur among women worldwide each year. It is the most common malignancy in women in developing countries.

Cancer cervix is considered to be an ideal gynaecological malignancy for screening, as it meets both test and disease criteria for screening. It has a long latent phase during which it can be detected as identifiable and treatable malignant lesions, which precede the invasive disease and the benefit of conducting screening for carcinoma cervix exceeds the cost involved.

The efficacy of cervical smear study was established by George N Papanicolaou. [11]

Since cytology is the examination utilized for the screening of cervical cancer, it is important to determine its correlation with histologic examination, the gold standard in the diagnosis of cervical disease. [2]

The Bethesda system for reporting cervical cytological diagnosis is a uniform system for reporting and it is useful to provide effective communication among cytopathologists and referring physicians. [2]

## MATERIALS AND METHODS

The study was performed on 100 cases on women between the age group of 18 to 70 years for a study period of October 2012 to September 2014, presenting with complaints of white discharge per vaginum, pain abdomen and menstrual irregularities.

After a detailed clinical examination, Pap smears were obtained and stained with Papanicolaou stain. The conventional Pap smears were interpreted according to The Bethesda System 2001.

Hysterectomy and cervical biopsy specimens were processed and stained using H&E stain. The histopathology findings were reported and correlated with the cytological findings. The sensitivity, specificity and positive predictive value were calculated of Pap smears and compared.

## RESULTS

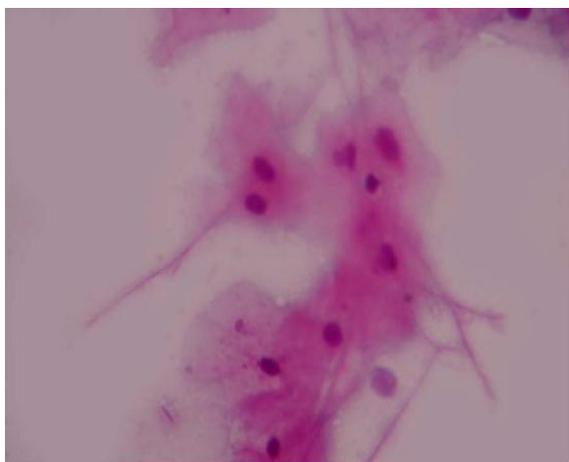


Figure 1: Candida Albicans- Showing Pseudo hyphae (Pap, 40x).

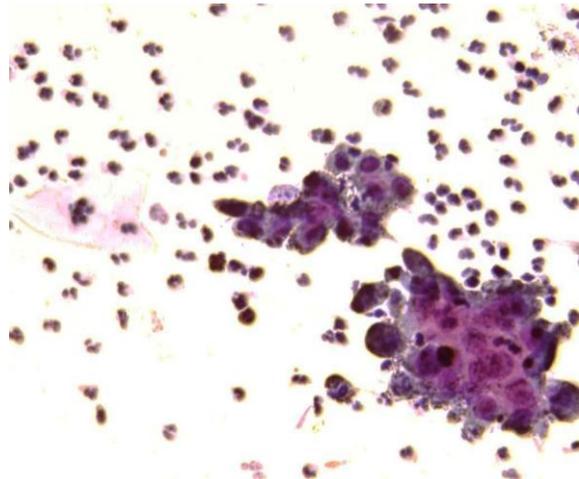


Figure 2: Reactive cellular change- Clusters of reactive Para basal cells with prominent nucleoli in an inflammatory background. (Pap, 40x).

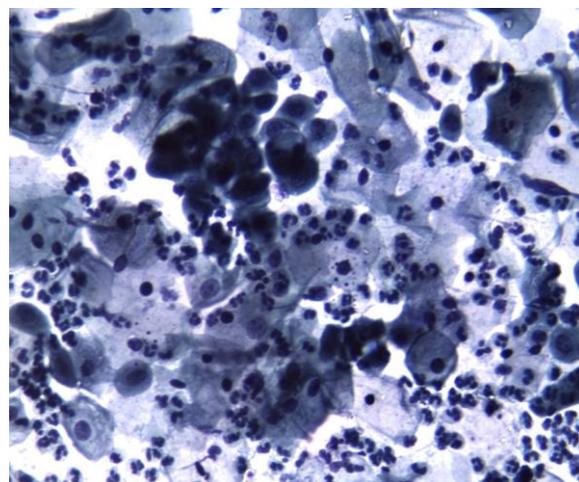


Figure 3: LSIL- Intermediate cells arranged in clusters showing increased nuclear cytoplasmic ratio (Pap, 40x).

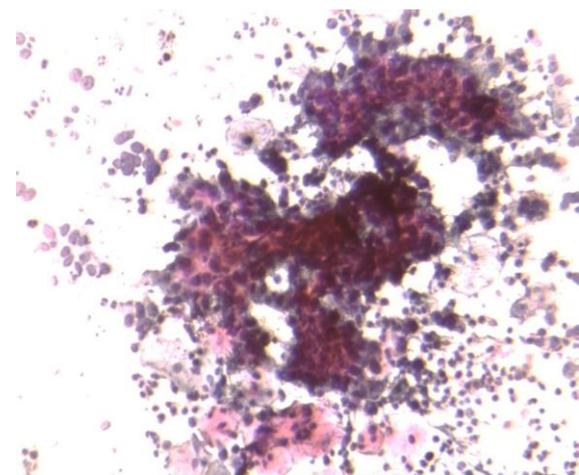


Figure 4: HSIL- Showing crowding of nucleus of the mature squamous epithelial cells. (Pap, 10X).

Most cases reported were in the age group of 31-40 years with median age at diagnosis was 34 years (range 18-70 years). Most of the cases of LSIL and HSIL were seen in fourth decade and carcinoma was

seen in fifth decade. The most common presenting complaint was white discharge per vagina constituting 55%, followed by irregular bleeding in 21%, pain abdomen in 15% and postmenopausal bleeding in 9%. Neoplastic lesions presented with pain abdomen, irregular bleeding and post menopausal bleeding.

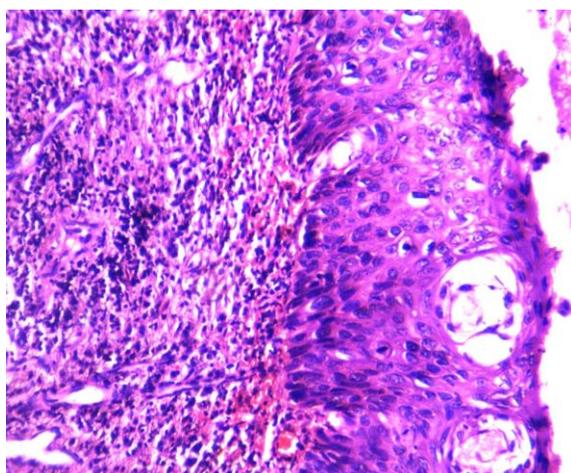


Figure 5: Koilocytes- LSIL/CIN I showing koilocytic change in the epithelium.

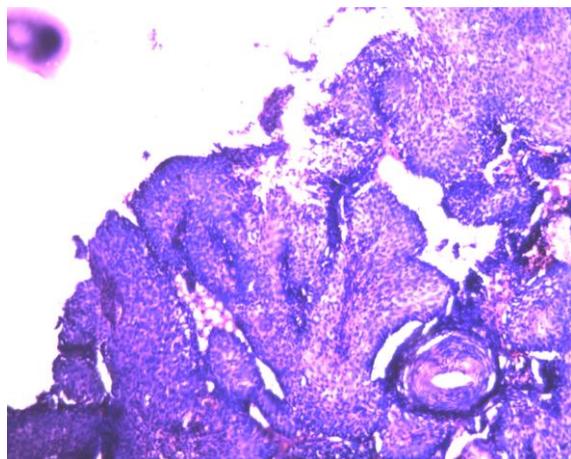


Figure 6: HSIL/CIN III- Showing dysplastic cells involving entire thickness of epithelium. (H&E, 10X).

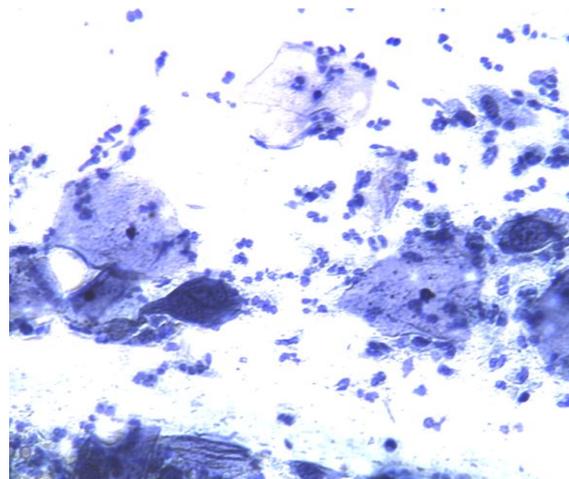


Figure 7: Squamous cell carcinoma- Showing pleomorphic cells with irregular nuclei. (Pap, 40X).

Out of total 100 cases, 77 cases were diagnosed as NILM, 2 cases were diagnosed as ASCUS, and 15 cases were given as LSIL, 5 cases as HSIL and only 1 case as Squamous cell carcinoma. Among negative for intraepithelial lesions or malignancy, nonspecific inflammation was most common comprising 63.6% followed by Reactive changes comprising 19.4%. Among the Organisms, Trichomonas vaginalis was common comprising 9.0% and least reported cases were Candida. Atrophic vaginitis comprised about 3.8%. On histopathology majority of cases reported were non neoplastic comprising 85% and neoplastic lesions comprised of 15%. Under neoplastic lesions, LSIL was most commonly reported followed by HSIL and carcinoma case.

Cytologic diagnosis of 100 cases using Bethesda System 2001

	NILM	ASCUS	LSIL	HSIL	SCC	AGC	AGUS	AC	TOTAL
No. of cases	77	2	15	5	1	-	-	-	100
Percentage	77%	2%	15%	5%	1%	-	-	-	100%

The concordance rate for non neoplastic lesions was 92.2% and for neoplastic lesions was 80.9%. Of the non neoplastic lesions, the diagnostic accuracy for inflammatory cases was 83.6% and in the remaining conditions like reactive changes, Organisms like Trichomonas and Candidiasis accuracy was 100%. Among

neoplastic lesions, diagnostic accuracy of LSIL was only 66.6%. Of the 15 LSIL cases 5 case were over diagnosed on cytology, which were reported as nonspecific specific cervicitis (2 cases) and polyoidal cervicitis (2 cases) on histopathology; whereas 1 case of LSIL was under diagnosed on cytology,

which was reported as HSIL/ CIN III on histopathology.

The sensitivity was 71.4%, specificity was 89.8% with Positive predictive value of 65.25 and negative predictive value of 92.2%.

## DISCUSSION

The incidence of cervical cancer has decreased more than 50% in the past 30 years because of widespread screening of cervical cytology. The mean age in the present study was 34 years which was comparable with the study of Julia H.C. et al [3] (35 years) and with the study of Vaghela et al [4] (36.7 years).

Adequacy of a sample: The Bethesda System defines a fully satisfactory specimen as containing both squamous cells and endocervical or squamous metaplastic cells. In the present study, all 100 Pap smears reported were satisfactory. [5] Negative for intraepithelial lesion or malignancy: The Bethesda System has introduced Negative for intraepithelial lesion or malignancy (NILM) as the new terminology. 77 cases were reported as NILM. Among them, majority were nonspecific inflammation (63.6%), followed by reactive cellular change (19.3%) and organisms in 10% cases. ASCUS: Determining whether to classify a specimen as NILM or ASC-US may be difficult in the

presence of inflammatory or degenerative changes, air-drying with nuclear enlargement, and other artifacts. 2 cases were reported as ASCUS on cytology, while on histopathology it was reported as polypoidal endocervicitis with no significant concordance. Sodhani et al [6] observed that of total 60 ASCUS cases, 56 cases showed chronic cervicitis, while 4 cases showed CIN 1 lesion on histology.

In The Bethesda System, low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL) encompass the spectrum of precursors to squamous cell carcinoma cervix. 15 cases were diagnosed as LSIL on cytology. While on histopathology, 10 cases turned out to be LSIL and remaining were diagnosed as nonspecific cervicitis (2 cases), polypoidal cervicitis (2 cases) and HSIL (1 case) on histopathology. The discrepancy can be attributed to accumulation of dense inflammatory infiltrate showing reactive atypia and sampling errors. 5 cases were diagnosed HSIL on Cytology, out of which 4 cases were reported as HSIL on histopathology. Only one case was diagnosed as squamous cell carcinoma on cytology in the present study, which correlated well on histopathology. Similar findings were reported by a study done by Bhalerao A et al. [7]

Comparison of concordance rate for neoplastic lesions

Study	Cytology diagnosis	Histopathology diagnosis	Percentage
Bodal KV et al	200	79	87.3%
Pradhan B et al	25	22	88%
Present study	21	15	71.4%

The concordance rate for neoplastic lesions was 71.4% in the present study. Bodal K.V. et Al [8] found 87.3% of concordance rate. Pradhan B et al [9] found concordance rate of 88%.

The diagnostic accuracy in the present study for non neoplastic lesions such as inflammatory cases was 83.6%, reactive change and organisms was 100% each. For neoplastic lesions, carcinoma had diagnostic accuracy of 100%, followed by HSIL (80%)

and LSIL (66.6%). Study done by Saha et al [10] found diagnostic accuracy of 79.1% for benign cases, 100% for carcinoma, 90.7% for HSIL and 86% for LSIL cases. Anschuet al [11] suggested that it is important to review cytology and histology slides for the purpose of guaranteeing greater diagnostic accuracy in the laboratory. Smears from invasive lesions are difficult to interpret and often under diagnosed. [12]

Comparison of sensitivity and specificity with various studies

Studies	Sensitivity	Specificity	Positive predictive value
Amaral G.R.et al <sup>[13]</sup> (2005)	73.5%	98.6%	64.1%
Jain V.et al(2007) <sup>[14]</sup>	78%	26.9%	91.1%
Saha R.et al(2005) <sup>[15]</sup>	60%	93.9%	75%
Present study	71.4%	89.8%	65.2%

The high specificity (89.8%) can be attributed to the slides being reviewed, both cytology and histopathology only once. In the present study, 28.6% of false negative rate was observed. The failure in cytologic interpretation can be due to error in the processes of sampling, clinical alterations of the patients, such as the period of the menstrual cycle in which the examination was performed, the presence of leucorrhoea or bleeding and even the presence of comorbidities which can influence the sampling. False negative rate can be decreased by using a proper technique to sample the smears, rapidly fixing the slides to prevent air drying and subsequent artifacts in the slides, as well as ensuring good quality control in the laboratory. The false positive rate in the present study accounted to 1.4%, which can be attributed to interpretative error in the face of cervicitis, repair or metaplasia being interpreted as CIN or Carcinoma.

## CONCLUSION

Thus as cervical cancer has defined premalignant phase of many years, we can use Pap smear and histopathology for early diagnosis and treatment, to decrease morbidity and mortality associated with carcinoma of cervix. The Pap smear has good sensitivity and specificity and positive predictive value in detecting high grade lesions and malignancy. The sensitivity for cervical intraepithelial neoplasia is low but it can be increased by adequate sampling and avoiding technical errors like air drying and fixation artifacts. The discrepancy can be minimized by following The Bethesda system for adequacy of sampling.

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