

Histopathological Vs. cytological findings in cervical lesions (Bethesda System 2001) – A comparative study

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Abstract

Background: Cervical malignancy is the major health burden in India. For detection in early stage, the screening test is PAP smear. To check the sensitivity and specificity of Bethesda system, the cytological findings have to be correlated with histology considering histopathology as gold standard.

Objective: To study usefulness of cytology in detecting various cervical lesions, to evaluate and interpret the cases of epithelial lesions and correlation of cytological findings with subsequent follow-up histology sections.

Materials and Methods: A retrospective review of PAP smears in Dhiraj General Hospital in the period from May 2015 to September 2016. They were correlated with corresponding follow-up biopsies using revised 2001 Bethesda System. Analysis of different factors causing discrepancies was done.

Results: The PAP smear has overall sensitivity of 86.04%, specificity 42.85%, positive predictive value 90.24 %, negative predictive value 33.33 % and accuracy 80% in detecting low/high grade lesions and malignancy.

Keywords: Cervical cytological findings; Histopathological findings; Correlation; Bethesda system.

1. Introduction

The Bethesda system for reporting cervical cytological diagnosis is a uniform system for reporting & it is useful to provide effective communication among cytopathologists & referring physician. The conventional Papanicolaou (PAP) smear, embraced by clinicians since the 1940s, came into widespread use in the 1950s as a means of detecting carcinoma of the female reproductive tract, particularly cervical carcinoma and its precursors.[1]

Cervical cytology is mainly performed as a screening test in women who underwent hysterectomy owing to lower genital tract neoplasia or, in a small percentage, which have a current lesion in the vaginal mucosa [2,3]. The present study was conducted to study the usefulness of cervical and vaginal cytology in diagnosis of pre-neoplastic and neoplastic lesions of cervix. Though not ideal, a retrospective study was carried out in an attempt to determine whether a serious problem existed in our laboratory, which can be corrected.

1.1 Aims and Objectives

- ❖ Correlation of cytological findings with follow-up histology sections.
- ❖ To evaluate and to interpret the cases of epithelial lesions according to the Bethesda 2001 classification system.
- ❖ Scrutiny of different factors causing discrepancies in final diagnosis.
- ❖ Addition of an aid to internal quality control.

2. Methods and Material

Using the Conventional Papanicolaou (PAP) method, smears were taken by gynaecologist in gynaecology OPD, Dhiraj General Hospital over a period from May 2015 to September 2016.

Personal information & clinical history like age, parity, religion, use of tobacco, socio-economic status, chief complaints, HIV status, any previous treatment (hormonal /surgery /radiotherapy) taken for carcinoma cervix was noted. The age range of the subjects varied from 20 to 70 years with parity between 0 to >5.

All the smears were made by scrapping the endocervix from the squamo-columnar junction with the cotton swab stick by rotating the swab stick in clockwise direction and fixed straightway with ethyl alcohol fixative for 30 minutes. All procedures were performed by gynaecologist. They were sent along with fully filled requisition form to cytology lab for further processing. All fixed slides were stained by Papanicolaou stain.

The smears showing epithelial abnormality and the follow up biopsy were studied retrospectively. Histology slides were stained with H& E stain. Correlation of cytological findings with histological counterpart was done and concordance rate was calculated for each entity considering cytology as the gold standard. All the reporting of PAP smears was done according to The Bethesda 2001 classification system & for histology WHO classification system 2003 was used. Comparison of present study results was done with other similar studies in the past.

2.1 Cytological Interpretation

According to the Bethesda system 2001, the gold standard method for cervical cytology, all the cervical lesions are categorized as follow [4,11,13].

2.2 Negative for intraepithelial lesion or malignancy (NILM)

(When there is no cellular evidence of neoplasia, state this in the General categorization above and/or in the Interpretation/Result section of the report- whether or not there are organisms or other non-neoplastic findings)

Organisms:

- *Trichomonas vaginalis*
- Fungal organisms morphologically consistent with *Candida* spp.
- Shift in flora suggestive of bacterial vaginosis
- Bacteria morphologically consistent with *Actinomyces* spp.
- Cellular changes consistent with herpes simplex virus

2.3 Other non-neoplastic findings (Optional to report; list not inclusive):

- Reactive cellular changes associated with
 - inflammation (includes typical repair)
 - radiation
 - intrauterine contraceptive device (IUD)

Glandular cells status post-hysterectomy Atrophy

2.4 Other

- Endometrial cells (in a woman ≥ 40 years of age) (Specify if “negative for squamous intraepithelial lesion”)

2.5 Epithelial Cell Abnormalities

1. Squamous Cell

- Atypical squamous cells
 - of undetermined significance (ASC-US)
 - cannot exclude HSIL (ASC-H)
- Low-grade squamous intraepithelial lesion (LSIL) (Encompassing: HPV/mild dysplasia/CIN 1)
- High-grade squamous intraepithelial lesion (HSIL)

(Encompassing: moderate and severe dysplasia, CIS; CIN 2 and CIN 3)

- with features suspicious for invasion (if invasion is suspected)

- Squamous cell carcinoma

2. Glandular Cell

• Atypical

- Endo-cervical cells (NOS or specify in comments)
- Endo-metrial cells (NOS or specify in comments)
- Glandular cells (NOS or specify in comments)

• Atypical

- Endo-cervical cells, favour neoplastic
- glandular cells, favour neoplastic
- Endo-cervical adenocarcinoma *in situ*

• Adenocarcinoma

- Endo-cervical
- Endometrial
- Extra-uterine
- Not otherwise specified (NOS)

2.6 Statistical Analysis

In present study, the overall sensitivity was 86.04%, specificity 42.85%, positive predictive value 90.24 %, negative predictive value 33.33 % and accuracy 80%.

Calculation:

Sensitivity = $\{A / A+C\} \times 100 = 86.04 \%$

Specificity = $\{D/D+B\} \times 100 = 42.85\%$

Positive predicted value = $\{A / A+B\} \times 100 = 90.24 \%$

Negative predicted value = $\{D/D+C\} \times 100 = 33.33 \%$

Accuracy = $\{A +D / A+B+D+C\} \times 100 = 80 \%$

[A= TP= True positive cases= 37

B=FP=False positive cases=04

C=FN= False negative cases=06

D=TN= True negative cases=03]

3. Results & Discussion

The cytology findings and corresponding histology findings were studied in all epithelial lesions. Cytology (PAP smears) was taken as the gold standard. They were classified according to the Bethesda 2001 system mentioned above and the histological findings were classified according to the WHO classification 2003[5].

The total number of smears throughout the duration of study was 250. Out of these, 170 smears were inflammatory/ benign, 30 were unsatisfactory (According to Bethesda exclusion criteria) and the remaining 50 smears showed epithelial cell lesions.

For all the epithelial cervical lesions, physicians were advised to perform follow up cervical biopsy for confirmation of diagnosis.

In present study, retrospective examination of histopathological finding of all the 50 epithelial lesions were done and compared with cytological PAP smear findings.

The overall concordance rate was calculated. Also for individual lesions, concordance rate was analysed according to the Bethesda System 2001. Majority of the cases were of Squamous cell carcinoma.

All lesions are categorized as following (Table-1).

Table: 1: Categorization of cervical epithelial lesions according to cytopathology and histopathology findings

Sr.No.	Epithelial cell lesions - Pap smear cytological findings (Total no of cases-250)	Epithelial cell lesions - pap smear histological findings (Total no of cases-50)	
		CIN I	CIN II/III
1	ASCUS (06)	08	-
2	ASC-H (08)	09	-
3	LSIS (06)	08	-
4	HSIL (12)	00	09
5	SCC (18)	00	14
6	Negative/Benign (170)	-	02

The overall concordance of the study was 76%. The discordant rate was 24%. (Table 2)

Table: 2: The overall concordance rate of the study

Cases	Number	Percentage (%)
Discordant	12	24
Concordant	38	76
Table	50	100

In the present study, the overall concordance rate was 76% which is comparable to other studies e.g. Study by Nawaz [6] (a study from Aga Khan University, Pakistan) where the concordance rate was 74%. The other studies like Saha's [7], Yeoh [8] & Rasbridge [9] has concordance rates as 60%, 52% and 81.2% respectively (Table 3).

Here, out of the 12 conflicting cases, 7 cases were under diagnosed on cytology, 3 cases were called as negative/benign and ASCUS, ASC-H & LSIL were the diagnoses in 1 case each. The main reason for underreporting was less cellularity with haemorrhagic/inflammatory obscuring background. Repeat smears from such patients showed actual diagnosis and upgraded accordingly. In such cases, biopsy was found to be the significant aid in the diagnosis. Few smears showed air drying and fixation artefacts and so the diagnosis was interrupted.

In Saha's study [7] & Yeoh's study [8], a major component of false negative rate appeared to be sampling and preparation artefacts. So the conclusion drawn was to decrease false negative rate, smears should be repeated at regular intervals. Error rate is negligible with three normal consecutive annual smears. It is appropriate to take the test with higher degree of abnormality as the correct result. [10]

Table 3: Comparison of overall concordance rate with other studies

Name of Study	Concordance Rate
Audit by Simon Rasbridge [9]	81.25
Yeoh Study [8]	52%
Saha's Study [7]	60%
Nawaz Study [6]	74%
Present Study	76%

The study by Nawaz [6] showed overall concordance rate of 74%. A total 8 numbers of cases were discrepant. The causes for discrepancies were mainly sampling error, air drying and blood or inflammation obscuring the cellularity.

In the study by Yeoh [8], total of 128 cases were diagnosed on histology as CIN II/III out of which 72 cases were concordant. Out of the remaining 56 cases, 52 were under diagnosed on cytology and 4 cases were over - diagnosed as squamous cell carcinoma. The concordance rate was 74.6%.

The concordance rates for Nawaz [6], Gupta and Sodhani [12] study were 92% and 74% respectively.

In the study by Gupta and Sodhani [12] titled as 'Why is high grade squamous intraepithelial neoplasia under diagnosed on cytology in a quarter of cases? Analysis of smear characteristics in discrepant cases cervical smears of 100 histology proven cases of cervical intraepithelial neoplasia III (CIN III) were retrieved and reviewed to study cytological agreement in high grade lesions. Cytology was able to correctly identify 74 HSILs whereas in 26 cases a diagnosis of LSIL or below was given on review, 16 of these cases were reclassified as HSIL on cytology while 10 cases showed persistent diagnosis of LSIL. 12/16 (75%) cases represented interpretative errors. Sampling error was 7/10 and air drying 5/10 were found in underdiagnosed cases.

4. Conclusion

The current study provides a hint to evaluate the internal quality of cytology reporting. The PAP smear has good sensitivity and specificity and positive predictive value in detecting high grade lesions and malignancy. The sensitivity can be increased by adequate sampling and avoiding technical errors like air drying and fixation artefacts. The inconsistency can be minimized by following the Bethesda system for adequacy criteria of sampling. The sampling and fixation artefact can be effectively reduced by proper coordination and discussing smear preparation problems with the physicians/ gynaecologist.

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