

Cytological versus Histopathological Examination in Lesions of Cervix, taking histopathology as a Gold Standard

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ABSTRACT

Background: Malignancy of cervix is the major health burden in South Asia including Pakistan. PAP smear is the screening test for its early detection. To find out the specificity and sensitivity of the system called as Bethesda system, the correlation of cytological findings with histopathology, with histopathological examination as the golden standard.

Aim: To find out the cytological utility in diagnosing different pathologies of cervix, to assess and infer the epithelial lesions cases and to correlate cytology findings with its consequent follow-up biopsies.

Methods: This study was carried out taking 150 PAP smears of women coming to gynecological OPD of Shaikh Zayed Hospital Lahore from September 2020 to February 2021. There correlation with subsequent follow-up histology sections by using 2001 revised Bethesda System. Different factors analysis which were causing inconsistencies was done.

Results: The overall sensitivity of PAP smear is 86.94%, specificity 57.14%, positive predictive value 86.94 %, negative predictive value 57.14 % and accuracy 80% in detecting low/high grade lesions and malignancy.

Keywords: Bethesda system, Cervix cytology findings; Histopathological findings.

INTRODUCTION

About ten lac women die around the globe in a year. Cancer of cervix is second most common among malignancies of female after breast carcinoma. This morbidity and mortality are reduced when diagnosed timely. The Bethesda system reporting cytology of cervix and diagnosing it, that is the unchanging system to report & provide a useful and efficient way of communication among cytopathologists & refer towards other doctors. The physicians incorporated conventional, old Papanicolaou (PAP) smear from the nineteenth century, which was being used widely and was brought into widespread use in the 1950s for detecting female genital tract malignancy, mainly carcinoma cervix and its precursor lesions.^[1] Cytology of cervix (PAP smears) is primarily done as a screening test for women which undergo total hysterectomy due to reproductive tract malignancy or, a small ratio, who have a recent pathology affecting vagina.^[2,3] The study that was carried out currently which was to study the effectiveness of cytology of vaginal and cervix to diagnose neoplastic and pre-neoplastic cervical pathologies.

Aims and Objectives

- To correlate findings of cytology with subsequent biopsy sections.
- To assess and interpret the epithelial lesion cases with reference to the Bethesda 2001 classification system.
- Enquiry of multiple factors which are causing inconsistencies in final ultimate diagnosis.
- An assistance to control the internal quality.

Received on 03-02-2021

Accepted on 23-05-2021

MATERIALS AND METHODS

With the help of Conventional Papanicolaou (PAP) method, we took smears from women aged above 25 years presenting in gynaecological OPD, Shaikh Zayed Hospital Lahore over a period from September 2020 to February 2021 by gynaecologist. Personal biodata & clinical symptomatic history like age, religion, parity, tobacco use, HIV status, socio-economic status, presenting complaints, any past therapy (surgery /hormonal /radiotherapy) taken for cervical carcinoma was taken and entered in a well-designed performa. The age of patients ranged from 25 to 70 years and parity between 0 to >5. All the smears were taken from transformation zone (squamo-columnar junction) of cervix by scraping it with the help of high vaginal swab stick rotate the stick at 360 degrees and directly fixed in ethanol fixative for 30 minutes. Then they sent them along with completely filled request form for further processing to cytology lab. In the lab, staining of fixed slides were done by Papanicolaou stain. The follow up biopsies were taken of the smears with abnormality in epithelium. Histology sections staining were done with the routine Hematoxylin & Eosin stain. Cytopathological examination and histopathological correlation were done and rate of concordance was calculated for each category. All PAP smears were reported as per The Bethesda 2001 classification system & for histological findings WHO 2003 classification system was used.

All the cytopathological lesions of cervix were classified as per guidelines of 2001 Bethesda system of cytology of cervix^{4,11,13}.

Negative for any intraepithelial lesion or malignancy (NILM)
(When there is no cytological finding of carcinoma/ neoplasias found in smears)

Organisms: Bacteria *Trichomonas vaginalis*, shows shift in flora which is consistent with bacterial vaginosis

- Fungal organisms morphology favor *Candida* species, Bacteria which morphologically resemble with *Actinomyces* spp.
- Cytological changes which favor herpes simplex virus 2.
- Other
- Findings of Endometrial cells (in a women greater than 40 years) (indicate if it is "negative for squamous intraepithelial lesion")

2.5 Abnormalities in Epithelial Cells

In Squamous Cells

- Atypical squamous cells of undetermined significance (ASC-US)
- Low-grade squamous intraepithelial lesion (LSIL) (focusing: Human Papilloma Virus / CIN 1)
- High-grade squamous intraepithelial lesion (HSIL) (focusing: moderate and severe dysplasia, CIN 2 and CIN 3; Carcinoma in situ)
- Squamous cell carcinoma

Glandular Cells

- Atypia (Endo-cervical cells / Endo-metrial cells / Glandular cells (NOS or specify in comments))
- Atypia cells (glandular cells / Endo-cervical cells which favors malignancy, and Endo-cervical adenocarcinoma in situ)
- Adenocarcinoma (Endometrial, Endo-cervical, Extra-uterine, Nostroispecific (NoS))

In present study Statistical Analysis says, that generally it was 57.14% specific, 86.95% sensitive, with 86.95% positive predictive value (PPV), 57.14% negative predictive value (NPV) and 80% Accurate

Calculation:

Specificity = $\{D/D+B\} \times 100 = 57.14\%$
 Sensitivity = $\{A/A+C\} \times 100 = 86.95\%$
 Negative predictive value (NPV) = $\{D/D+C\} \times 100 = 57.14\%$
 Positive predictive value (PPV) = $\{A/A+B\} \times 100 = 86.95\%$
 Accuracy = $\{A+D/A+B+D+C\} \times 100 = 80\%$
 [A= True positive (TP) = 20, B= False positive (FP) = 3, C= False negative (FN) = 3, D= True negative (TN) = 4]

RESULTS

The cytopathological results and subsequent histopathological results were examined and studied in all epithelial cell lesions. Histopathology was considered superior and was taken as the golden standard. The classification was done according to the system named as 2001 Bethesda classification system which was stated previously and the histopathological results were categorized as per WHO 2003 classification system⁵. Total 150 smears were included. Among these, 102 out of 150 smears were non-malignant/inflammatory, 18 cases were not satisfactory and in the residual cases, 30 revealed abnormalities in epithelial cells. All lesions of cervix with abnormalities in epithelial cells, clinicians were guided to take biopsy from the cervix for confirming the diagnosis. The overall rate of concordance was calculated. Also, the concordance rate was analyzed for all pathologic entities individually, according to the guidelines of Bethesda 2001 System. Squamous cell carcinoma was the most prevalent neoplastic pathology. All these pathologic lesions are classified as under in (Table 1).

Table 1: Categorization of epithelial cell lesions of cervix according to cytopathological and histopathological examination

Epithelial cell lesions – PA Psmr cytopathological results (n=150)	Epithelial cell lesions – PA Psmr histopathological results (n=30)	
	CIN I	CIN II/III
Atypia cell of undetermined significance (6)	6	-
Atypical squamous cell – H (4)	5	-
Low grade squamous cell carcinoma in situ (6)	6	-
High grade squamous cell carcinoma in situ (6)	0	7
Squamous cell carcinoma (8)	0	5
Non-neoplastic (102)	-	1

Generally, this study was 76% concordant and 24% discordant (Table 2)

Table 2: The rate of concordance

Cases	n	%age
Discordance rate	9	30
Concordance rate	21	70
Total	30	100

DISCUSSION

This study is 70% concordant with other such studies, for example. Study carried out by Nawaz⁶ at Aga Khan University, Pakistan showed 74% concordance. The other studies for example Rasbridge⁷, Yeoh⁸ & Saha⁹ & had concordance rates as 81.2%, 52% and 60% correspondingly.

In this study, out of the 9 conflicting cases, 5 cases were undiagnosed on cytopathology, 3 cases were diagnosed as non-neoplastic and ASCS, AC-H & LSL were the diagnoses in 1 case each. The major cause for underdiagnosis was low cellularity with haemorrhage/inflammation concealing background. Actual diagnosis was

made when such smears were repeated. Biopsy helped in these cases. Some smears showed fixation and air-drying errors and so the diagnosis was hindered. In studies by Yeoh⁷ & Saha⁸, a main factor of false negative rate was due to preparation and sampling errors. Thus, to conclude in order to lessen false negative rate, repeat smears should be taken at regular intervals. With three normal successive smears performed annually the Error rate is almost minimal.

CONCLUSION

The present research gives a clue to assess the interquality of cytological reporting. For the diagnosis of high-grade lesions and malignancies, the PAP smear is very specific, sensitive and has a good positive predictive value. The sensitivity can be amplified by satisfactory sampling and minimizing practical problems like fixation and air-drying

errors. The variation can be lessened by following sampling adequacy criteria of the Bethesda system. The fixation and sampling artefacts can be efficiently minimized by appropriate organization and conversing errors during smear preparation with the clinicians.

Source of support: nil

Conflict of interest: None

Conflict of interest notification page: All authors have no conflict of interest to any information or data in this study.

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