

Correlation of Epithelial Cell Abnormality in Cervical Cytology with Cervical Histology

Shrestha R¹, Sinha K², Sharma N², Shrestha A³

ABSTRACT

Introduction: Cervical cancer is the second most common cancer in females worldwide and third most common cancer in Nepal. Conventional Pap smear is the most widely used screening tool for detecting premalignant and malignant lesions of cervix. Cytohistological correlation of Pap smear is a widely accepted method for analysis of various factors leading to discrepancies in diagnosis and internal quality assurance. **Aim:** To study the cytohistological correlation of epithelial cell abnormality in Pap smear in Nepalgunj Medical College Teaching Hospital, Kohalpur, Banke, Nepal. **Methods:** This is a hospital based prospective cross sectional study carried out at Department of Pathology, NGMC, Kohalpur, Nepal from August 2018 to January 2020. The study included 137 cases of Pap smear with epithelial cell abnormality and correlated with corresponding histopathological findings. **Results:** The age of patients ranged from 20-80 years with the number of cases seen in the range of 30-39 years (n=44; 32.1%). Whitish discharge per vaginum was most common presenting symptom. High grade squamous intraepithelial lesion (HSIL) was the most common abnormal finding in Pap smear with a frequency of 40 (29.1%) cases. Out of 137 cases of Pap smear 57 (41.6%) cases showed discrepancies in cervical biopsy. All cases of Squamous Cell Carcinoma (SCC) were correctly diagnosed by Pap smear. The overall sensitivity of smear test was 84%. After evaluating cytohistological correlation, the Positive Predictive Value (PPV) was found to be 100% for SCC, 52% for HSIL and 59% for Low grade squamous intraepithelial lesion (LSIL). **Conclusion:** The current study revealed a good correlation between cervical cytology and biopsy in Pap smear showing epithelial cell abnormalities. Thus, cytology and histology are complementary to each other and helps to reduce discrepancies.

Keywords: Cytohistological correlation, High grade squamous intraepithelial lesion, Low grade squamous intraepithelial lesion, Pap smear

Authors:

1. Dr. Richa Shrestha
2. Dr. Kavita Sinha
3. Dr. Nirmala Sharma
4. Dr. Anil Shrestha

¹ Department of Pathology, Nepalgunj Medical College and Teaching Hospital, Kohalpur, Banke

² Department of Obstetrics and Gynaecology, Nepalgunj Medical College and Teaching Hospital, Kohalpur, Banke

³ Department of Medicine, Nepalgunj Medical College and Teaching Hospital, Kohalpur, Banke

Address for Correspondence:

Dr. Richa Shrestha
 Department of Pathology
 Nepalgunj Medical College and Teaching Hospital
 Kohalpur, Banke, Nepal
 Email: shrestharicha@hotmail.com

INTRODUCTION

Cancer of the cervix is the second most common cancer in developing countries following breast cancer and ranks fourth globally.¹ It is third common cancer in females in Nepal.² Human Papilloma Virus (HPV) is considered as the primary factor in the development of cervical cancer. Poor living condition, lack of hygiene, early age of first intercourse, multiple sexual partner are other etiological factors.³ Cervical cytology using the Papanicolaou (Pap) smear is most commonly used cervical cancer screening method in developing countries, despite of other advanced tests for high risk HPV, which is not available widely. A significant decrease in the incidence and mortality of

cervical cancer is due to effective cervical cytology screening program. Although cervical cytology is considered effective for screening of precancerous conditions of cervix, its false negative yield due to sampling and interpretation error is still a reason of concern. Thus histological correlation of Pap smear is one of the recommendations of the European guideline for quality reassurance to reduce false negative results.⁴

Thus the present study has been carried out to evaluate the cytohistological correlation of cervical lesion in Pap smears with epithelial cell abnormalities.

METHODS

This is a hospital based descriptive study conducted over the period of August 2018 to January 2020 in Department of Pathology, NGMC, Kohalpur, Banke, Nepal. Informed verbal consent from the patient and permission of the institutional review committee (IRC) of the hospital was also obtained. Total 137 Pap smears with epithelial cell abnormality were included in the study whose corresponding histopathological sample was also received in the form of cervical biopsy or hysterectomy performed for various indications. The study group included women of different age group who were attending gynecology outpatient department (OPD).

Inclusion Criteria

- Epithelial cell abnormality in Pap smear.
- Cervical biopsy on the corresponding patient for histopathological study.

Exclusion Criteria

- Negative for Intraepithelial lesion and Unsatisfactory smears for evaluation in Pap cytology.
- Epithelial cell abnormality in Pap smear without cervical biopsy of same patient.

The Pap smears were taken with the Ayer's spatula on a clean glass slide and fixed immediately in 95% ethanol and ether.⁵ Staining of the slides were performed by means of the conventional Pap technique and was reported according to the Bethesda for cervical cytology 2014 and biopsies were advised for correlation. Tissue sample obtained was fixed in 10% neutral buffered formalin and processed routinely with final embedding in paraffin blocks and stained with hematoxylin and eosin (H&E).⁶ Biopsy results were evaluated with the Cervical Intraepithelial Neoplasia (CIN) classification and the correlation with Pap smear was studied.

Biopsy reports were categorized as nonneoplastic (cervicitis, polyps and immature squamous metaplasia), CIN I (LSIL), CIN II and CIN III (HSIL) and Invasive carcinoma according to World Health Organization (WHO) classification.⁷ Pap smear cytology reports were categorized according to Bethesda for cervical cytology- 2014.⁸ Data were analyzed using Microsoft excel 2010 and standard statistical software SPSS 20.0.

RESULTS

A total of 137 cases were included in the study. All of them had abnormal Pap smear finding that fulfilled the epithelial cell abnormality criteria according to the Bethesda -2014. The peak age group was between 30-39 years (44 cases, 32.1%), as shown in table I. The mean age of the patient was 38.5. The most common presenting complain was whitish discharge per vagina (52%) followed by pain lower abdomen (40%). There were 37 (26.9%) cases of Low grade squamous intraepithelial

lesion (LSIL), 40 (29.1%) cases of High grade squamous intraepithelial lesion (HSIL), 30 (22%) cases of Atypical squamous cell of undetermined significance (ASC-US), 13 (9.6%) cases of Atypical squamous cells cannot exclude a high-grade squamous intraepithelial lesion (ASC-H), 7 (5.2%) cases of Atypical Glandular cells Not otherwise specified (AGCNOS), and 10 (7.3%) cases of Squamous cell carcinoma (SCC) on Pap smear cytology. On histopathology, there were 22 (16.1%) Nonneoplastic cases, 40 (29.1%) CIN I cases, 20 (14.7%) CIN II cases, 25 (18.2%) CIN III cases, 28 (20.4%) SCC and 2 (1.5%) Adenocarcinoma (Table II). Out of 30 cases of ASC-US, 16 was CIN I followed by 8 nonneoplastic cases on histopathology. Out of 37 LSIL in Pap smear, 22 was CIN I in biopsy. Including both HSIL and ASC-H (40 and 13 cases respectively), 27 were accurately diagnosed as CIN II and III in biopsy (11 and 16 cases respectively). All 10 SCC in Pap smear was diagnosed as invasive SCC in biopsy. Out of 7 AGCNOS, 2 were adenocarcinoma. The most common histopathological finding was CIN I (40 cases; 29.1%) followed by SCC and CIN III (28 cases; 20.4% and 20 cases; 14.7% respectively). The correlation of malignancy in Pap smear with histopathology was statistically significant with p value of <0.001. The sensitivity of cytology was 84% with false positivity of 16%. We were unable to calculate specificity, and negative predictive value as there were no real negative or false negative cases in cytology.

The correlation was calculated using Positive Predictive Value (PPV) in our study data and showed increased cytohistological correlation with CIN as the degree of epithelial cell abnormality increased. This was matched based on the Bethesda terminology counterpart of the smear result with CIN terminology of the biopsy result. The PPV was 100% for SCC, 52% for HSIL , 59 % for LSIL and 28% for AGCNOS (Table III). Out of 137 cases, 80 cases (58.4%) showed concordance between Pap smear and cervical biopsy while discrepancies was seen in 57 (41.6%) cases (Table IV).

Age (Year)	Frequency	%
20-29	8	5.9%
30-39	44	32.1%
40-49	37	27.0%
50-59	36	26.3%
60-69	11	8.0%
70-80	1	0.7%
TOTAL	137	100%

Table I : Distribution of ages groups

Pap Smear Diagnosis	Histopathological Diagnosis						Total	P Value
	Non-Neoplastic	CIN I	CIN II	CIN III	SCC	Adeno-carcinoma		
LSIL	8 (5.8%)	22 (16.0%)	7 (5.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	37 (26.9%)	<0.001
HSIL	2 (1.5%)	1 (0.7%)	7 (5.1%)	14 (10.1%)	16 (11.6%)	0 (0.0%)	40 (29.1%)	
ASCUS	8 (5.8%)	16 (11.7%)	4 (3.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	30 (22.0%)	
ASCH	0 (0.0%)	0 (0.0%)	2 (1.5%)	9 (6.6%)	2 (1.5%)	0 (0.0%)	13 (9.6%)	
AGCNOS	4 (3.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	7 (5.2%)	
SCC	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (7.3%)	0 (0.0%)	10 (7.3%)	
TOTAL	22 (16.1%)	40 (29.1%)	20 (14.7%)	25 (18.2%)	28 (20.4%)	2 (1.5%)	137 (100%)	

Table II: Correlation of Pap smear and histopathological diagnosis with P value

Cytopathological Diagnosis	Histopathological Diagnosis	PPV
LSIL	CIN I	59%
HSIL	CIN II & III	52%
SCC	SCC	100%
AGCNOS	Adenocarcinoma	28%

Table III: Positive Predictive Values of cyto-histopathologic diagnosis

Pap Smear Diagnosis	Concordant Cases	Discordant Cases	Total cases
LSIL	22	15	37
HSIL	21	19	40
ASCUS	16	14	30
ASCH	9	4	13
AGCNOS	2	5	7
SCC	10	0	10
TOTAL	80 (58.4%)	57 (41.6%)	137 (100%)

Table IV: Concordance and discordance cases between Pap smear and cervical biopsy

DISCUSSION

Most of the cervical cancer arises from the transformation zone, which can be detected by a good Pap smear. The Pap smear is regarded as an ideal screening tool worldwide for sexually active women.⁹⁻¹¹

Cervical Pap smear is a widely used screening test as it is simple and cost effective in developing countries like Nepal. The aim of cervical screening test is to enable early detection and treatment of precancerous and cancerous lesion and prevent mortality due to cervical cancer. However, it has a high false negative rate ranging from 1.1-30 %, as shown in various studies.^{12,13} This is due to variation in sampling technique, smear preparation and difference in impression among expertise. Thus, comparing cytological impression with cervical biopsy is considered as immediate gold standard method to reduce the false negative rate.

This study is done to enhance the role of Pap smear in gynaecology cytology and its correlation with biopsy which provides important information regarding resolving the discrepancies or confirming the diagnosis by histology.¹⁴ In the present study, maximum number of cases were in the age group 30-39 years (41 cases), which is similar to studies done by Bamanikar SA et al, Likhari KS et al, Kaveri SB et al and Joshi et al.¹⁵⁻¹⁸ Whitish discharge per vaginum was the most common presenting symptom as reported in other similar studies.¹⁶⁻¹⁸ In this study, HSIL was the most common abnormal finding in Pap smear with 29.1% of all smears examined. Similar observations were made by Shah R et al¹⁹ and Fatima NK et al¹⁴, followed by LSIL in 37 (26.9%) and ASCUS in 30 (21.2%). Most common histopathological diagnosis among women with abnormal Pap smear was CIN I which accounted for 40 (29.1%) of cases. Similar finding was observed in other studies.^{3,14,18,20-22} All 10 cases of SCC on PAP smear were diagnosed as invasive SCC in histopathology. Similar observation was made by Fathima NK et al¹⁴, Joshi C et al¹⁸, Abali R et al²⁰ and Poudel A et al.²¹

We found nonneoplastic changes in 8 cases, CIN I in 16 cases, CIN II in 4 cases and CIN III in 2 cases of total 30 ASC-US cases. The total rate of CIN among cases with an ASC-US smear result was 73%. The cases with ASC-H diagnosis in PAP smear was diagnosed as CIN II in 2 cases, CIN III in 9 cases and SCC in 2 cases by biopsy. The higher rate of CIN in cases reported as ASC-US and ASC-H in Pap smear indicated a need of close follow up and cervical biopsy in these patients. This observation was also seen in a study done by Abali R et al.²⁰ The false positive cases in this study showed chronic cervicitis or inflammation related regenerative changes which increased the rate of smear reported as ASC-US.

This study showed increased cytohistological correlation with Cervical Intraepithelial lesion as the degree of epithelial cell abnormality increased in Pap smear which is similar to study done by Abali R et al.²⁰ In this study, concordance and discordance between Pap smear and histopathology is 58.4% and 41.6%, with the increased concordance rate, which is also seen in study done by Poudel A et al²¹, Jain RV²² and Jyothi R et al.²³

LIMITATIONS

Limitation of this study is that all the biopsies were not performed using colposcopy, which could cause error in identifying most suspicious area of cervix for taking biopsy and histopathological study resulting in false negative diagnosis. Thus colposcopy and colposcopy guided biopsy of cervix should be used along with Pap smear for increasing the accuracy of detection of cervical lesion.

CONCLUSION

Pap smear is an ideal screening test for detection of precancerous and cancerous cervical lesion. However, under certain conditions, it may give false positive impression of neoplasia. Thus, it is necessary to perform a cervical biopsy which is considered to be the gold standard in cases of epithelial cell abnormality in Pap smear. The current study result supported a good correlation between cervical cytology and histopathology concluding that conventional Pap smear is a cost effective, simple and quick method of detection of precancerous and cancerous cervical lesion.

REFERENCES

- GLOBOCAN 2018 (IARC), Section of cancer information (12/9/2018) WHO, 2018; GLOBOCAN 2018 database, IARC.
- Population based cancer registry in Nepal, IARC, Interim analysis of data, Nov 2018.
- Patil PR, Jibhkate SN. Cytohistopathological correlation of Papanicolaou smears: a hospital based study. *Int J Reprod Contracept Obstet Gynecol* 2016;5:1695-9.
- Wiener, HG, Klinkhamer P, Schenck U, Arbyn M, Bulten J, Bergeron C, et al. European guidelines for quality assurance in cervical cancer screening: recommendations for cytology laboratories. *Cytopathology*. 2007;18(2):67-78.
- Koss LG, Melamed MR. *Koss Diagnostic Cytology and its histopathological bases Vol I*. 5th ed America: Lippincott 2006; 1591-93.
- Bancroft DJ. *Theory and Practices of Histological Techniques*. 7th ed. India: Elsevier; 2013. p 105-123.
- Rosai J. *Rosai and Ackerman's surgical pathology*. Vol II, 10th ed London: Elsevier 2011; 1444-57.
- Nayar R, Wilbur DC. *The Bethesda system of reporting cervical cytology*. 3rd ed USA: Springer 2015; xiii-xv.
- Imtiaz F, Hasa WHG, Klinkhamer P, Schenck U, Arbyn M, Bulten J, et al. European guidelines for quality assurance in cervical cancer screening: recommendations for cytology laboratories. *Cytopathology*. 2007;18(2):67-78.
- Saslow D, Runowicz CD, Solomon D, Moscicki AB, Smith RA, Eyre HJ, et al. American Cancer Society Guidelines for the early detection of Cervical neoplasia and cancer. *CA Cancer*. 2002; 52:342-62.
- Sawaya GF, Brown AD, Washington AE, Garber AM. Clinical practice: current approaches to cervical cancer screening. *N Engl J Med*. 2001; 344:1603-7.
- Chhabra Y, Behera BG, Khalkho J, Pati N. Cytomorphological study of PAP smears in precancerous And cancerous lesions. *J Cytol* 2003; 20(2):64-7.
- Ozkara SK, Yildiz K. Retrospective five year analysis of our cervicovaginal cytology screening programme under the perspective of Bethesda-2001. *Turkish Bulletin of Pathology*. 2002;19:119-24.
- Fathima NK, Patil AM, Patil S, Sajjanar BB, Yendigeri SM, Arifulla K. Cyto- histological correlation of cervix lesion. *UJMDS* 2016, 04 (01): 28-30.
- Bamanikar SA, Baravkar D, Chandanwale S, Dharwadkar A, Paranjape S. Study of cervical cytology and its correlation with clinical and histopathological findings. *Clin Cancer Investig J* 2016;5:403-8
- Likhar KS, Saluja A, Gupta SG, Hazari RA, Likhar SK. Precancerous and cancerous lesions of cervix diagnosed by Pap's smear – A hospital based study. *J Evol Med and Dent Sci* 2014;3:1899-904
- Kaveri SB, Khandelwal S. Role of Pap smear *N* cervical biopsy in unhealthy cervix. *J Sci Innov Res* 2015;4:4-9
- Joshi C, Kujur P, Thakur N. Correlation of Pap Smear and Colposcopy in Relation to Histopathological Findings in Detection of Premalignant Lesions of Cervix in A Tertiary Care Centre. *Int J Sci Stud* 2015;3(8):55-60.
- Shah R, Thapa M. Correlation of cervical cytology with cervical histology. *Kathmandu Univ Med J (KUMJ)* 2005, Jul-Sep;3(3):222-4.
- Abali R, Bacanakgil BH, Celik S, Aras O, Koca P, Boran B, Dursun N. Histopathological Correlation of Squamous Cell Abnormalities Detected on Cervical Cytology. *Turkish Journal of Pathology* 2011; 27(2): 144-148.
- Poudel A, Dahal P. Cytohistological correlation of conventional Papanicolaou smears in cervical neoplasia at a tertiary care hospital of Nepal. *J Pathol Nep* 2019;9:1475-9.
- Jain RV. Screening for Carcinoma Cervix with Simultaneous use of PAP smear, colposcopy guided cervical biopsy-A prospective study. *Pariplex -Indian journal of research*. 2018;6(4):7-8.
- Jyothi R, Gupta P, Rao R, Sood PL, Parasher N. Correlation between Colposcopy, Cytology and Histopathology in High-risk Patients for Cervical Cancer in Perimenopausal Women in Himachal Pradesh, India. *Journal of SAFOMS*. 2013;1:21.