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Original Article

Epithelial Cell Abnormality in Cervical Pap Smear with Histopathological Correlation among Patients of a Tertiary Care Centre in Eastern Nepal

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Abstract

Background

Cervical cancer is a leading health problem among women all over the world with significant mortality and morbidity in developing countries like Nepal. Pap smear is an effective and cost efficient diagnostic technique for cervical lesions. This study aims at histopathological correlation of cervical Pap smears.

Materials and Methods

A cross sectional study was conducted from January 2020 to January 2022 in Pathology department of Nobel Medical College Teaching Hospital (NMCTH). Cases of cervical Pap smear were reported using the Bethesda system and correlated with histopathological examination findings for various epithelial cell abnormalities. Analysis was done using SPSS software version 20.

Results

Out of 5110 smears examined, 119 were positive for epithelial cell abnormalities. Cellular abnormality was commonly seen between 31-60 years of age. Low grade Squamous Intraepithelial Lesion was the commonest lesion found. Pap smear findings had good concordance rates with histopathological findings for individual lesions. The overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of Pap smear were 84%, 23.1%, 89.9%, 15% and 77.3% respectively.

Conclusion

Pap smear has a good diagnostic accuracy, sensitivity and positive predictive value in diagnosing cervical lesions in comparison to histopathological examination.

Keywords: *Cervical Cancer,Cytology, Pap smear*

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Introduction

World Health Organization states cervical cancer as one of the commonest cancer in females worldwide, having significant mortality and morbidity especially in developing countries [1, 2]. Cervical cancer is one of the commonest malignancies among women of Nepal [3]. Therefore cervical cancer is a serious leading health issue in women worldwide [4].

Early detection of cervical cancer in pre-invasive stage is helpful for reducing disease associated burden. This can be facilitated by Pap smear screening which is a simple, non-invasive, cost effective and sensitive test for early detection of variety of lesions of cervix. The widely accepted reporting system for the Pap smearis The Bethesda System (TBS) 2001[5].

Present study aims at detecting various patterns of cervical epithelial abnormalities by Pap smear examination. Similarly the accuracy of diagnosis by Pap test will be tested by correlating it with histopathological examination.

Materials and Methods

This is a cross sectional study done in Pathology department of Nobel Medical College Teaching Hospital, Biratnagar, Nepal from January 2020 to January 2022. Ethical approval for the study was obtained from Institutional Review Committee of NMCTH. Convenience sampling method was applied. All the women who are sexually active and visiting gynecological OPD with complaints of vaginal discharge, vaginal bleeding and something coming out of vagina were included in the study after obtaining informed expressed consent. Unmarried females, pregnant women and known case of cervical cancer were excluded from the study. The sample size was calculated by the formula $N=Z^2pq/d^2$ where Z=1.96 (95%CI), d=degree of accuracy required (5% error), p=proportion in the targeted population estimated to have a particular characteristics (50% for maximum sample size)) and q= 1-p. The calculated sample size was 384 and convenient purposive sampling method was used. However, we considered the entire sample (5110) received in the laboratory for this study in the study period.

Properly labeled pap smears, fixed in 95% ethyl alcohol, of the respective females were received along with detailed history from gynecology department. The smears were then subjected to pap stain, mounted with DPX, examined and reported as per Bethesda system 2001. Subsequently cervical biopsy specimens that were received in formalin containing bottle werefixed for 12 hours. Then tissue were embedded and kept in processing device for 24 hours. Wax blocks containing tissue were made and sections prepared in glass slides with the help of microtome. Tissue sections were stained with Hematoxylin and Eosin stain, mounted and examined under microscope. The histopathological findings were then correlated with cytological findings.

All the findings were noted in standard proforma. The data analysis was done using SPSS software Version 20. Pap findings were correlated with histopathological findings to find out sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of pap smears. Values were derived separately for individual diagnosis as well as for overall sample.

Results

Total of 5110 smears were examined from January 2020 to January 2022. Out of them74 were found to be inadequate for evaluation due to presence of blood and mucus. 4917 (97.63%) smears were found Negative for Intraepithelial Lesion or Malignancy (NIELM). Remaining 119 (2.37%) smears showed epithelial cell abnormalities of various kinds and were subsequently followed up for histopathological findings.They contained Atypical Squamous Cell of Unknown Significance (ASCUS), Low grade Squamous Intraepithelial Lesion(LSIL), High Grade Squamous Intraepithelial Lesion (HSIL), Squamous Cell Carcinoma (SCC) and Adenocarcinoma (AC). Age of the patient ranged from 15–80 years. Majority of the patient were under 40 years of age. Most common epithelial cell abnormality was LSIL followed by HSIL, SCC and ASCUS. Single case of adenocarcinoma was diagnosed. Overall epithelial lesions were more common before 50 years of age (Table 1).

Table 1: Age wise distribution of various epithelial cell abnormalities of cervix diagnosed by Pap smear

	Age group						
Cytology	15-30	31-40	41-50	51-60	61-70	>71	Total
NIELM	2105 41.79%	1739 34.53%	521 10.34%	422 8.37%	108 2.14%	22 0.43%	4917 97.63%
ASCUS	2 0.04%	3 0.05%	6 0.11%	4 0.07%	1 0.01%	4 0.07%	20 0.39%
LSIL	0	14 0.27%	21 0.41%	5 0.09%	4 0.07%	0	44 0.83%
HSIL	0	8 0.15%	16 0.30%	4 0.07%	2 0.04%	0	30 0.59%
SCC	0	4 0.07%	12 0.23%	8 0.15%	0	0	24 0.46%
AC	0	0	0	1 0.01%	0	0	1 0.01%
Total Percent	2107 41.83%	1768 35.46%	576 11.43%	444 8.81%	115 2.28%	26 0.51%	5036 100%

The Pap smear findings were further correlated with histopathological findings. According to the Bethesda reporting system,2001; the LSIL

correspondsto the Mild dysplasia /(Cervical Intraepithelial Neoplasia) CIN I. Similarly HSIL corresponds to moderate and severe dysplasia; CIN2 and CIN3 along with Carcinoma in situ (CIS) respectively (Table 2).

Table 2: Correlation of Pap smear and histopathological diagnosis

Cytology	Histopathology						
	Chronic cervicitis	CIN I	CIN II	CIN III / CIS	SCC	AC	Total
ASCUS	32.52%	12 10.08%	5 4.20%	-	-	-	20 16.80%
LSIL	108.40%	20 16.80%	14 11.76%	-	-	-	44 36.97%
HSIL	-	3 2.52%	8 6.72%	15 12.60%	4 3.36%	-	30 25.21%
SCC	-	-	-	2 1.68%	22 18.48%	-	24 20.16%
AC	-	-	-	-	-	1 1%	1 1%
Total	13 10.92%	35 29.41%	27 22.68%	17 14.28%	26 21.84%	1 1%	119 100%

The concordance rates were 57.1%, 52.3%, 84.6%, 100% and 84% for LSIL, HSIL, SCC, Adenocarcinoma and overall lesions respectively. Pap was least sensitive in diagnosing HSIL (52.3%) and also the Negative Predictive Value (NPV) was least (76.7%). Positive Predictive Value (PPV / 45.5%) and Diagnostic Accuracy (67.22%) were least for LSIL. For overall lesion NPV was only 15% and Specificity only 23.1%. The overall pattern revealed that Pap was more correlated with histopathology with increasing degree of epithelial dysplasia. Overall diagnostic accuracy was 77.3% (Table 3).

Table 3: Statistical values of Pap smear for various abnormal epithelial lesions in percentage

Statistical values	LSIL	HSIL	SCC	AC	Overall lesions
Sensitivity	57.1	52.3	84.6	100	84
Specificity	71.4	90.7	97.8	100	23.1
Positive Predictive Value	45.5	76.7	91.7	100	89.9
Negative Predictive Value	80	76.7	95.8	100	15
Diagnostic Accuracy	67.22	76.47	94.96	100	77.3

Table 4: Comparisons of statistical parameters with other studies

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	DA (%)
Malpani G et al [10]	86.61	73.33	96.49	39.29	85.21
Chaudhary R et al [14]	25.40	99.27	94.12	74.32	76
Rashmi S et al [16]	33.33	92.59	68.89	75	67.57
Ashmita D et al [17]	19.51	83.33	80	86.54	23.26
Shah R et al [18]	76	83.3	86.4	71.4	79.1
Present study	84	23.1	89.9	15	77.3

Discussion

Cervical cancer is one of the commonest malignancies in females occurring throughout the world having greatest mortality in low income nations [6]. The exact data regarding the prevalence of cervical cancer is not known in Nepal but it is among the commonest malignancy in Nepalese women as per report annual (2018) of BP Koirala memorial cancer hospital [7]. Pap screening has been established as one of the gold standard test for cervical cancer screening. It has helped in significant amount to reduce cancer related mortality [8]. Poor record system has led to improper estimate of cervical cancer cases. Each year there are 2332 new cases with mortality rate of 1367. Lack of vaccination against Human Papilloma Virus (HPV), difficult geographical location for easy delivery of health servicesand lack of proper health facility has all led to difficulties in fighting cervical cancer [9].

In present study the epithelial cell abnormality was seen in 119 (2.37%) out of 5036 cases. This was similar to the finding of Malpani G et al (2016) who had such anomaly in 144 (2.04%) cases[10]. Worldwide prevalence of such cellular abnormality is in range of 0.98% to 15.5%. Multiple risk factors involved, sample size taken for analysis and different criteria used from diagnosis could be some of the reasons for this variation. About 90% of the patient having epithelial cell abnormality was between 30-60 years age group. This wasin accordance to the finding of Ranabhat S et al (2011) who found out 76% cases above the age of 30 years in a study done in Mid-western Nepal. Similarly 80% of all epithelial cell abnormality was found above the age of 41 years which coincided with this study [11]. Present study revealed 41-50 years age group having maximum number of epithelial cell abnormalities (46%) which was in accordance to findings of Naik R et al (2015) who reported same age group for similar findings [12].

Among all lesions LSIL was the most common epithelial cell abnormality (36.9%) followed by HSIL (25.2%) and SCC (20.1%). There was only one case of adenocarcinoma with 100% concordance with histopathology. Other studies like Malpani G et al, Gupta K et al (2013) and Chaudhary RD et al (2014) had also shown similar observations of LSIL being the commonest [10, 13, 14].However,Ranabhat S et al found HSIL as the most common lesion [11]. The difference in observation among these studies is probably due to the variation in cases which each of them have encountered.

The overall specificity of pap,for diagnosis of cervical lesions, was quite low in present study (23.1%). However these values were quite good for individual lesions. Unlike present study others have good specificity [14, 15, 16] The overall sensitivity (84%) was comparable to findings of Malpani G et al who had sensitivity of 86.61% [10]. Otherstudies had low sensitivity of Pap smear in diagnosing cervical lesions [14, 15].

Similarly PPV was good with all the studies. Again NPV was low for present study and Malpani G et al [10]. Diagnostic accuracy was (77.3%) in present study which was similar study done by Rachana LY et al (2017) where it was found to be 87.95% [17]. Hence present study shows good correlation between Pap smear and cervical histology with respect to individual lesions as well for overall lesions in terms of sensitivity, PPV and diagnostic accuracy.

Conclusion

Pap smear has a good diagnostic accuracy, sensitivity and positive predictive value in diagnosing cervical lesions in comparison to histopathological examination. It can be used as an invaluable tool for early and easy detection of cervical lesions.

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Conflict of interest: None

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