

Correlation of Cervical Pap Smear with Biopsy in the Lesion of Cervix

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ABSTRACT

Background

Cervical cancer can be controlled to a greater extent by screening to improve morbidity and mortality. Pap smear is important screening method, which has proven to be highly effective in reducing the number of cases and the mortality from cervical carcinoma. Any abnormality detected in pap smear has to be confirmed with cervical biopsy, which remains the reference investigation.

Objective

To find the changes of cervical cytology by pap smear, to classify cervical lesions into malignant and benign groups on cytological and histopathological basis and to correlate the changes observed in cervical cytology with cervical biopsy.

Method

This is a prospective cross sectional study done in between July 2014 and July 2015 in Dhulikhel Hospital, Kathmandu University Hospital. During the period, all the samples requested for pap smear were studied. The cases who had undergone both pap smear and cervical biopsy were compared. Clinical data were obtained from requisition submitted along with the cytology and tissue specimens received in the department.

Result

During the study period, total 1922 pap smears were performed and out of them 75 patients were advised to do cervical biopsy. On cytology, out of total 1922 number of cases, 67.90% were normal, 27.90% were inflammatory smears, 3.80% were unsatisfactory (inadequate) and 0.40% were high grade intraepithelial lesions. Highest numbers of patients screened for pap smear ranged from 31 to 40 years. On histopathology, 78.70% had chronic cervicitis, 8% had normal findings, 1.30% had moderate and 6.70% had severe squamous intraepithelial lesions. The frank malignancy was found in 5.30%. The mean age \pm SD for carcinoma was 52.75 \pm 6.29. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value of pap smear were 77.80%, 100%, 100% and 97% respectively considering cervical biopsy as the gold standard

Conclusion

This study revealed a good correlation of cervical cytology with cervical biopsy. Pap is a cost effective screening method for early detection of premalignant and malignant cervical lesions. However, biopsy is considered as the gold standard for the confirmation of abnormalities detected in cervical smear.

KEY WORDS

Biopsy, cervix, pap smear

INTRODUCTION

Cervical cancer is the most common cause of cancer related death in women, and it is the second most common cancer after the breast cancer worldwide.¹ In developing countries, cervical cancer comprises 90% of all genital malignancies.²

Cervical cancer is preventable and curable, if detected early or in pre-invasive stages.³ Premalignant lesions of cervix commonly involve transformation zone of the uterine cervix. The histopathological terminologies used to describe grades of the disease are: low grade CIN (cervical intraepithelial neoplasia) comprises CIN I lesions with koilocytic atypia and, high grade CIN consist of CIN II and III. Mild dysplasia (CIN I) in histopathology corresponds to low-grade squamous intraepithelial lesions (LSIL) in cytology whereas moderate and severe dysplasia (CIN II and CIN III) in histopathology corresponds to high grade intraepithelial lesions (HSIL) in cytology. The high grade lesions are true precursors of invasive cancer.^{3,4} Cervical cytology is a widely used technique for cervical cancer screening.⁵ Pap's test is a cytodiagnostic tool, which is highly accurate in predicting the presence of cervical neoplasia.⁶ Pap smear has been substantiated by several studies in the last 50 years,^{7,8} and this method has resulted in decreasing the incidence and the mortality rates of cervical cancer in the developed world.^{9,10}

But pap alone cannot determine the location of abnormality. Hence, cervical biopsy remains the 'gold standard' for the diagnosis of cervical pre cancer when the cellular details are obscured by blood in pap's test.¹¹

The objectives of the study were to find out the changes of cervical cytology by pap smear, to classify cervical lesions into malignant and benign groups on cytological and histopathological basis and to correlate the changes observed in cervical cytology with cervical biopsy.

METHODS

This is a prospective cross-sectional study done in the Department of Pathology at Dhulikhel Hospital, Kathmandu University Hospital during the period of July 2014 and July 2015 after receiving ethical clearance from institutional review committee (IRC). During the period, all the samples requested for pap smear were studied. The cases who had undergone both pap smear and cervical biopsy were compared. A total 1922 pap smear were performed. Seventy five cases underwent both Pap test as well as biopsy. Clinical data were obtained from requisition submitted along with the cytology and tissue specimens received in the department. The fixed cervical smears were subjected to staining according to Papanicolaou's method. The cytological interpretation of the smears was made according to the new 2001 Bethesda system.¹² Cervical biopsies received were undergone grossing and were processed by routine paraffin techniques. The sections

stained with Haematoxylin and Eosin was taken for microscopic examination. For the difficult cases, the second opinion was taken from another experienced pathologist.

RESULTS

In this study, the age for screening cervical lesions by papanicolaou method ranged from 21 to 74 years. Between the age groups of 31 to 40 years, the highest numbers of pap smear were done. HSIL were commonly encountered in between 41 to 50 years (Table-1).

Table 1. Age wise distributions of the subjects with cervical pap smear findings.

Age groups (years)	Normal cytology	Inflammatory smear	Inadequate	HSIL	Total	%
21-30	390	173	14	1	578	30.1
31-40	461	190	28	1	680	35.4
41-50	294	112	19	3	428	22.3
51-60	124	47	7	1	179	9.3
61-70	31	13	6	0	50	2.6
>71	5	1	0	1	7	0.4
Total					1922	100

On cytology, out of 1922 cases, 1305 (67.90%) were normal, 536(27.90%) were inflammatory smears, 74(3.80%) were unsatisfactory, and 7(0.40%) were HSIL (Table-2). Among 536 inflammatory smears, 46(8.59%) had candidiasis and 490(91.41%) had non specific inflammation.

Table 2. Cervical cytological findings.

Pap smear findings	Number	Percentage (%)
Normal cytology	1305	67.9
Inflammatory smear	536	27.9
Inadequate	74	3.8
HSIL	7	0.4
Total	1922	100

Seventy five cases had both pap smear and cervical biopsy. Maximum number of cases on biopsy had non specific chronic cervicitis, which comprised of 59(78.70%). Normal studies were found to be six (8%). Moderate (CINII) and severe squamous intraepithelial lesions (CINI) were 1(1.30%) and 5(6.70%) respectively. The frank malignancy on biopsy was squamous cell carcinoma and adenocarcinoma, which comprised of 3(4%) and 1(1.30%) respectively (Table-3). The mean age \pm SD for carcinoma was 52.75 \pm 6.29.

Out of 40 cases with normal cytology, six had normal histology and 34 had chronic cervicitis. On pap smear, 28 inflammatory smears were diagnosed out of which 25 had chronic cervicitis, one had CINII and two were carcinoma. There were seven HSIL cases diagnosed in smear out of which five had CINI and two had carcinoma (Table-4).

The calculation of sensitivity, specificity, positive predictive value and negative predictive value of a test depends on the definition of the ‘disease state’ that separates ‘positive’ from ‘negative’. The report of CINII, CINIII, squamous cell carcinoma and adenocarcinoma are considered as positive for the purpose of statistical analyses, the overall sensitivity, specificity, positive predictive value and negative predictive value and their values obtained were 77.80%, 100%, 100% and 97% respectively considering cervical biopsy as the gold standard. (Table 5)

Table 3. Histopathological findings of cervical biopsies

Cervical biopsy	Number	Percentage (%)
Chronic cervicitis	59	78.7
Normal	6	8.0
CIN III	5	6.7
SCC	3	4.0
CIN II	1	1.3
Adenocarcinoma	1	1.3
Total	75	100

Table 4. Correlation between cervical cytology and cervical biopsies

Cervical Cytology	Histopathological findings of cervical biopsy				
	Normal	Cervicitis	CIN II	CIN III	Carcinoma
Normal (40)	6	34	0	0	0
Inflammatory smear (28)	0	25	1	0	2
HSIL (7)	0	0	0	5	2

Table 5. 2*2 table of cytology and histology findings for detecting malignancy

Cytological Diagnosis	Histological Diagnosis		Total
	Positive for malignancy	Negative for malignancy	
Positive for malignancy	7	0	7
Negative for malignancy	2	66	68
Total	9	66	75

DISCUSSION

Cervical cancer screening is important to decrease morbidity and mortality. Various attempts are implemented to improve efficacy of cervical cancer.¹³ Premalignant lesions of cervix can be detected early and are also treatable before it proceeds into invasive disease. Hence, screening cervical cancer also benefits from the excessive cost involved.¹⁴

After the introduction of the pap smear by George Papanicolaou in 1947, cervical cytology has become the main diagnostic tool for the detection of cervical pathology.¹⁵ Due to easy availability, cost effectiveness and reliability; cervical smears have become a valuable tool

in screening and diagnosing various pathologies of the cervix.¹⁶

Various reports have mentioned the sensitivity of cytology for detecting cervical neoplasia that ranged from 50% to 98%.¹⁷ There are different methods that are being studied to improve the accuracy of cervical screening such as colposcopy, cervicography, etc. But biopsy has been considered as the gold standard for detecting cervical cancer.¹⁸ In this study we have compared cytological findings with cervical biopsy in the lesions of cervix.

After becoming sexually active, women are advised to have their first test and subsequently every 1 to 5 year. The American Cancer Society, National Cancer Institute, American College of Obstetrics and Gynecologists recommend that all women who are sexually active above the age of 18 years should have annual pap smear for three years.^{19,20} If three consecutive negative pap smears are found then the test can be extended in between the interval of 3 to 5 years. Similarly, the Canadian Task Force report recommended that sexually active women should have a cervical smear every 3 years after two negative smears.²¹

In this study, maximum numbers of patients were in between the age group 31 to 40 year, which comprised of 35.4%, followed by 30.1% between 21 to 30 years. This was similar to the study done by Boicea et al. which was done at Romania, and the maximum numbers of patients were in between 30 to 39 years, which comprised of 32.6%.²²

Cervical cancer is the second most common cancer in women, comprising of approximately 12% of all cancers, and being the most common in developing countries.²³ Globally, 500,000 new cases are diagnosed annually and 280,000 women die of the disease.²⁴ According to a regional study, cervical cancer comprises of 85% of all gynecologic malignancies in Nepal.²⁵

In this study, patients had the cytological diagnosis of 95.8% inflammatory/normal smears and 0.4% HSIL. This is comparable to the study of Yeoh et al. in which benign cases were 96% and HSIL were 0.5%.²⁶

In the context of histopathological findings in this study, out of 75 patients, on whom pap smear and biopsy were taken, 78.7% had chronic cervicitis, 8% had dysplasia, and 5.3% had malignancy. In a study done by Saha et al. out of 43 patients, on whom Pap smear and biopsy were taken, 55.8% had chronic cervicitis, 37.2% had dysplasia, and 6.97% had malignancy.²⁷ The mean age of patients with cancer was 52.75 years in our study population which is similar to the study of Bodal et al. (51.94 years) in Indian population.²⁸

The positive predictive value of pap smear was 100% in the present study. This was comparable to the study by Anschau et al. and Chhabra et al. in which the PPV were 90.9% and 92.8% respectively.^{29,30}

In the present study, sensitivity and specificity of pap smear were 77.8% and 100% respectively considering cervical biopsy as the gold standard. The sensitivity was comparable to the study done by Chhabra et al. and Jain V et al. which were 81% and 78% respectively.^{30,31} Similarly, specificity was comparable to Tamboli et al. which revealed 90.3%.³²

In cytology, false negative results for precancerous and cancerous lesions were due to inadequate sampling, due to technical errors like air drying and fixation artifact, inflammation and obscuring of the cellular details by blood.

CONCLUSION

Pap smear is a cost-effective and simple method for early detection of premalignant and malignant cervical lesions. The present study observed that cervical cytology was more specific in diagnosing cervical neoplasia. The cytological and histopathological findings were significantly correlated in the lesions of cervix. Adequate sampling and avoiding technical errors such as air-drying and fixation artifacts can increase the sensitivity of cervical intraepithelial lesion. Cytology and histopathological correlation are the important parts of quality improvement and even for the better evaluation.

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