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Association of Epithelial Cell Abnormality in Pap Smear Cytology with Histopathology

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ABSTRACT

Background

Cervical cancer is the fourth most common cancer among female globally while in Nepal it is the second most common cancer among female. Papanicolaou (PAP) test is a cytological screening technique which is simple, non- invasive and effective method for detection of pre-cancerous and non- cancerous lesions in cervix. The pre invasive phase of cervical carcinoma has a long course thus early identification in its precursor state is beneficial. This study aims to study association between pap smear cytology and histopathology in the cases reported as epithelial cell abnormality in cytology.

Methods

Cross sectional study was conducted over the period of 5 years at Department of Pathology, COMS-TH, Nepal. Cases with both pap smear cytology and its corresponding histopathology diagnosis were included in the study. Study of association between cytology and histopathology was done.

Results

Total of 82 cases of epithelial abnormalities on cytology were included with corresponding histopathology. ASCUS was the commonest abnormality reported accounting for 48.8% of cases. ASCUS, LSIL,ASC-H, HSIL and SCC had concordance of 77.5%, 62.5%, 46.15%, 40%, 100% respectively with histopathology. The association of epithelial abnormalities in Pap smear cytology with histopathology was statistically significant with p-value of <0.001.

Conclusions

Pap smear is cost-effective, easily available method of cervical cancer screening. It has excellent correlation with histopathological diagnosis. Thus, cervical cancer screening program should be conducted widely to decrease the cancer burden. Furthermore, cases of ASCUS or ASCH should be followed up by biopsy and adjunctive tests whenever necessary.

Keywords: epithelial abnormalities; pap smear cytology; histopathology.

INTRODUCTION

Cervical cancer is the fourth most common cancer among female globally.[1] In Nepal it is the second most common cancer accounting for 17.8% of total cancer incidence among female.[2] Human Papilloma Virus (HPV) is considered as the primary risk factor for cervical cancer.[3] Papanicolaou (PAP) test is a cytological screening technique which is simple, safe and non- invasive method for detection of pre-cancerous changes in cervix.[4] Pre invasive phase of cervical carcinoma has a long course thus early identification and treatment is beneficial.[5] Ancillary tests like HPV genotyping are not easily available in developing countries hence cytology is still the main screening method.[6] Whereas cervical biopsy is the gold standard test for definitive diagnosis.[7] Cyto-histologic correlation is helpful to refine diagnostic criteria as well as improve diagnostic accuracy.[8,9] Thus this research aims to study cytomorphological spectrum of epithelial cell abnormalities and establish its association with histopathology.

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METHODS

This is a hospital based analytical cross sectional study conducted over the period of 5 years from August 2019 to August 2024 in Department of Pathology, College of Medical Sciences Teaching Hospital, Bharatpur, Chitwan Nepal. Ethical approval was taken from institutional review committee (IRC) of the CoMSTH (Ref no. 2024-042). Cases with cytological diagnosis of epithelial cell abnormality and its corresponding histological diagnosis. i.e 82 cases were included in the study. Cases diagnosed as Negative for intraepithelial lesion/malignancy (NILM) were excluded. The conventional pap smears were reported according to the Bethesda system for reporting cervical cytology 2014 [10] and categorized in categories of epithelial abnormalities as:

Atypical squamous cells-undetermined significance (ASCUS), Atypical squamous cells- cannot exclude high grade squamous intraepithelial lesion (ASC-H), Low grade squamous intraepithelial lesion (LSIL), High grade squamous intraepithelial lesion (HSIL), Squamous cell carcinoma (SCC), Atypical glandular cell (AGC). Conventional pap smears which were wet fixed and stained with Papanicolaou stain were retrieved for cytological study. The tissue biopsy reports were categorized as non-neoplastic (cervicitis, polyps and metaplasia)[11], pre neoplastic as: CIN I (LSIL), CIN II(HSIL) and CIN III (HSIL) and invasive carcinoma according to World Health Organization (WHO) classification of female genital tumors.[12] Formalin fixed paraffin embedded sections stained with hematoxylin and eosin stain were retrieved for histopathological study. Data was entered in MS-Excel, refined and analyzed by using SPSS 20. Descriptive and inferential statistics were used for data analysis. Categorical variable wer presented uing frequency and percentage and chi-square test were used for comparison. p-value<0.05 was considered as statistically significant.

RESULTS

Out of total 2952 pap smears cytology 104 cases i.e 3.5 % were diagnosed as epithelial abnormalities. While 82 cases had histological follow up and were included for statistical analysis. Common age group of presentation with epithelial abnormalities was 40-50 years accounting for 33% of cases followed by 30-40 years accounting for 28% of cases as represented in Table 1.

Table 1. Age group distribution in cytology.

Age group	Frequency (%)
20-30	6(7.3%)
30-40	23(28%)
40-50	27(33%)
50-60	14(17.1%)
>60	12(14.6%)

Clinical presentation: Per vaginal discharge was the commonest clinical presentation followed by lower abdominal pain and per vaginal bleeding accounting for 71%, 24% and 5 % of total cases respectively. Frequency of epithelial abnormalities in cytology is demonstrated in Table 2.

Table 2. Frequency of epithelial abnormalities in cytology.

Pap smear Cytology	Frequency (%)
ASCUS	40(48.8%)
LSIL	16(19.5%)
ASCH	13(15.9%)

Cytological and histopathological correlation of epithelial abnormalities is tabulated in Table 3.

Table 3. Cytological and histological correlation of epithelial abnormalities.

Cytology	Histopathology			
	LSIL	HSIL	SCC	Others
ASC-US (40)	31(77.5%)	-	-	9(22.5%) (chronic cervicitis)
LSIL (16)	10(62.5%)	3(18.75%)	-	3(18.75%) (Chronic cervicitis)
ASC-H (13)	2(15.4%)	6(46.15%)	2(15.4%)	3(23%) (Atrophic changes)
HSIL (10)	1(10%)	4(40%)	5(50%)	-
SCC (2)	-	-	2(100%)	-
AGC (1)	-	-	-	1(100%) (Chronic cervicitis with atrophic changes)

The concordance rate of cytological and histopathological diagnosis in different categories are as follow: ASCUS = 77.5%, LSIL= 62.5%,

ASC-H=46.15%, HSIL=40%, SCC=100% with overall concordance of 62.5% as demonstrated in Table 4.

Table 4. Concordance of cytological-histopathological diagnosis.

Variables	Percentage (%)
ASCUS	77.50%
LSIL	62.50%
ASC-H	46.15%
HSIL	40%
SCC	100%

The association of epithelial abnormalities in Pap smear cytology with histopathology was statistically significant with p value of <0.001.

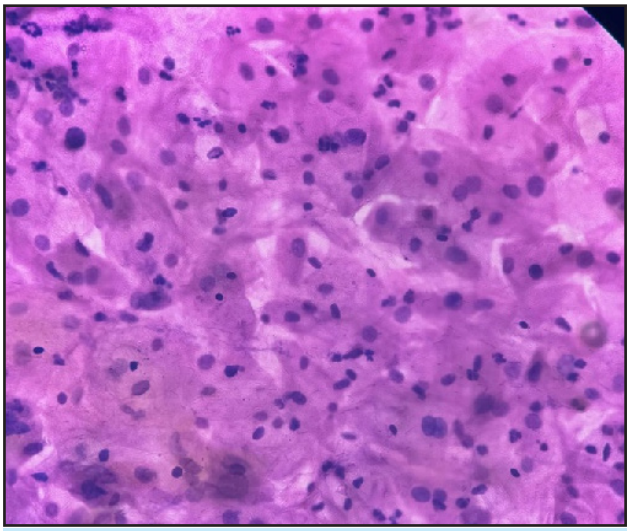

Figure 1. ASCUS on cytology.

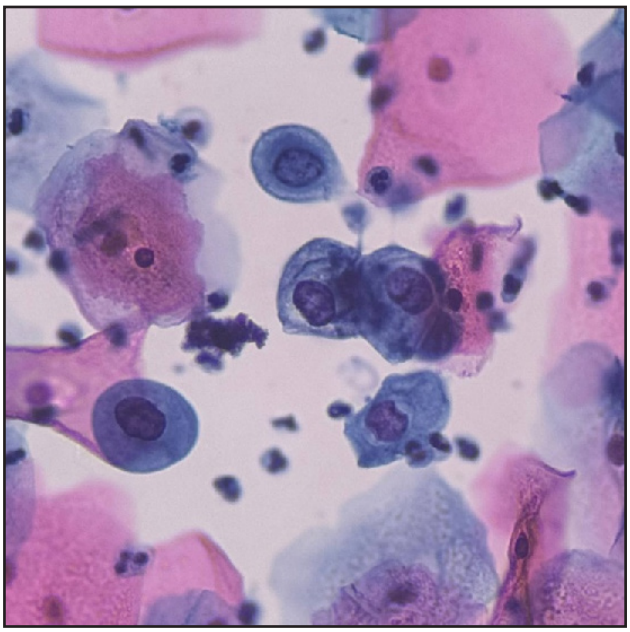

Figure 2. LSIL cytology.

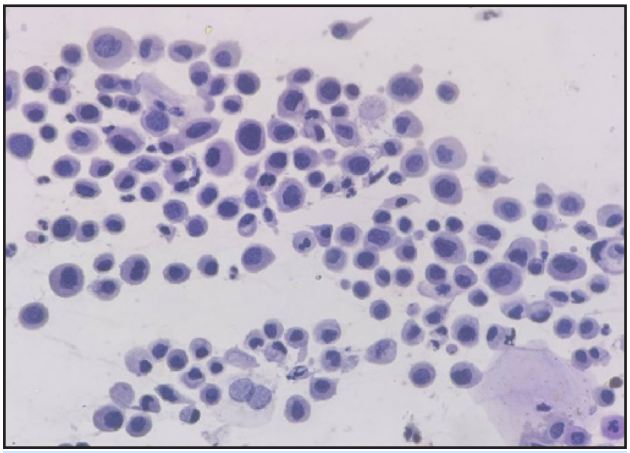

Figure 3. HSIL cytology.

DISCUSSION

Carcinoma cervix is one of the common cancer worldwide. It is the second most common cancer among female in Nepal with mortality rate of 8.9%.[2] It has a long latent phase during which it can be detected as identifiable and treatable premalignant lesions which precede the invasive disease.This period of latency is beneficial for conducting screening of carcinoma cervix.[13] Cervical Pap smear cytology is a widely used screening test as it is simple and cost effective in developing countries. 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.[14] Therefore periodical cytological screening helps in early detection of cervical lesions and help in reducing the morbidity and mortality associated with cervical cancer. [15] 2952 pap smears cytology were examined over period of five years in which 104 cases i.e 3.5 % were diagnosed as epithelial abnormalities. Similar prevalence of epithelial abnormalities ranging from 2.03-2.37% were noted on study by Malpani et al and Das et al.[15,16] Most common age group of presentation was 40-50 years with similar findings in study by Malpani et al, Das et al.[15,16] While few studies show higher frequency in age group of 30-40 years.[14] Per vaginal discharge was the most common clinical presentation followed by lower abdominal pain with similar findings in studies by Shrestha et al and Bamanikar et al.[14,17]

Among epithelial abnormalities ASCUS was the usual finding followed by LSIL, HSIL, ASC-H,

SCC and AGC. ASCUS accounted for 48.7% cases. Similar findings were noted in study by Poudel et al.[18] Whereas difference in high prevalence of LSIL among epithelial abnormalities were seen in studies by Malpani et al, Verma et al, Laxmi RC et accounting for 28.16%, 41.7% and 49.43% respectively.[15,19,20] While higher incidence of HSIL were reported by Shrestha et al and Dhakal et al.[14, 21] In histological follow up of the cases with epithelial abnormalities, among 40 cases of ASCUS 31 cases (77.5%) were diagnosed as LSIL and 9 cases (22.5%) as chronic cervicitis.

Among 13 cases diagnosed as ASCH on cytology 6 cases (46.15%) were diagnosed as HSIL, 2 (15.4%) as LSIL, 2 malignant (15.4%) i.e; 1 as SCC and 1 as adenosquamous carcinoma. 3 cases (23%) were diagnosed as atrophic changes. In index study increased frequency of cases as LSIL or higher abnormalities on histology which were reported as ASCUS and ASC-H on cytology warrents a close clinico-pathologic follow up. Adjunctive tests like HPV DNA should be performed whenever available on these categories of atypia. Similar findings were concluded in study by Shrestha and Abali et al.[14,22] Cases of epithelial abnormalities on cytology and negative in biopsy were mainly inflammatory and atrophic cases. The cytomorphological changes associated with atrophy in cervical cytology might mimic high-grade squamous intraepithelial lesion (HSIL). Thus, in setting of atrophy there may be cytomorphological over interpretation as ASC-H or HSIL.[23] There forth this feature must be considered while reporting the postmenopausal/ atrophic smears.

Also, 16 cases diagnosed as LSIL in cytology turned out to be LSIL(62.5%), HSIL(18.75%) and chronic cervicitis(18.75%). Around 63% cases of LSIL were correctly diagnosed with similar findings in study by Poudel et al.[18] While 19% of cases were upgraded and diagnosed as HSIL. 10 cases were diagnosed as HSIL on cytology which on histological follow up were SCC(50%) HSIL(40%) and LSIL(10%). Lack of features of invasion i.e tumor diathesis in cytology were considered for downgraded diagnosis as HSIL in the cases which were histologically proven as SCC. 2 cases diagnosed as SCC on cytology were both SCC on histology as well. 100% concordance of SCC diagnosis on cytology was also noted by Shrestha et al, Poudel et al and Abali et al.[14,18,22] 1 case diagnosed as AGC turned to be cervicitis with atrophic changes on histology. Detection of glandular abnormalities is very less in comparison to squamous component by pap smear. And presence of ambigious cytomorphology features of glandular component may be one of the reason for detection difficulty.[24] In this study about 65.2% had concordant cytology-histology correlation in total. Similar concordance rates were seen in study by Shrestha et al, Poudel et al,Abali et al and Shrestha B et al.[14,18,22,25]

CONCLUSIONS

Pap smear cytology is a well established screening method for detection of cervical cancer and its precursors. Detection of epithelial abnormalities with significant concordance rate further emphasize its use. Nevertheless, the categories of atypia in cytology (ASCUS/ASCH) needs periodical follow up and adjunctive investigations as there were significant rate of detection of precursor or malignant lesions in these categories of atypia as well.

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