Present Potential of Exfoliative Cytology in Detection of Cervical Cancer: Pattern of Epithelial Cell Abnormality

Sushila Jain,[a,c] Anuj Poudel,[a,d] SK Jain[b,d]

ABSTRACT:

Introduction: Conventional Pap smear is the mainstay for cervical cancer screening in developing countries and women should be motivated for cervical screening program to detect early dysplastic cells. This study was carried out to find out the prevalence of abnormalities in Pap smears, particularly pattern of epithelial cell abnormality in women attending Lumbini Medical College in western Nepal. **Methods**: A cross-sectional study was carried out and 1066 Pap smears were studied to look for epithelial cell abnormality according to revised Bethesda system 2001. **Results**: Out of 1066 patients who underwent Pap smear examination, 71 (6.6%) revealed epithelial cell abnormality; most were low grade squamous intra-epithelial lesions (LSIL) occupying 4.59% at the age between 23 to 29 years. Squamous cell carcinoma was found in 0.37 % of patients at the age 40 years and above. In our scenario, per vaginal discharge was the major finding of the patients who showed premalignant features. **Conclusions**: Women above 40 years are at a risk of premalignant as well as malignant lesions and these women should undergo screening for abnormal cells at the age of 18 or when sexual activity starts and as per recommendations to look for early dysplastic cells. Cervical screening program should be motivated by the national policy makers and also by health professionals.

INTRODUCTION:

Invasive carcinoma of uterine cervix, regardless of type, develops from precursor lesion or abnormal surface epithelium, which in its classic form, is known as carcinoma in situ. Precursor lesions do not produce any specific alteration of the cervix visible to the naked eye so these lesions earlier were a rarity to diagnose. Since the introduction of mass screening by smears, these lesions are quite common. For the detection of premalignant lesions of the cervix in a developing country and low resource setting, Pap smear test is one of the best methods.[1]

According to the Bethesda system 2001 for reporting, epithelial cell abnormality originates either from the squamous or glandular cells. In the category of squamous cells are ASC-US (Atypical squamous cells of undetermined significance) and ASC-H (Atypical squamous cells cannot exclude high grade intraepithelial lesions). The positive predictive value for HSIL (High grade squamous intraepithelial lesion) in ASC-H is higher than ASC-US but lower than HSIL.[2,3] Term squamous intraepithelial lesion (SIL) is subdivided into low grade which show perinuclear halo and mild dyskaryosis, and lesion showing moderate to severe dyskaryosis and carcinoma in situ, term HSIL. Smears showing

a - Lecturer
b - Professor
c - Department of Gynecology and Obstetrics, LMCTH
d - Department of Pathology
    Lumbini Medical College Teaching Hospital (LMCTH), Palpa, Nepal

Corresponding Author:
Dr. Sushila Jain
e-mail: sush18in@yahoo.com

no epithelial abnormalities are depicted under the category of negative for intraepithelial lesion or malignancy in the revised Bethesda system.[4,5]

Screening with Pap smear has seen to be accompanied by a dramatic reduction in the incidence of invasive cancer. Though liquid base cytology is popular, conventional Pap smear test is the main stay in the developing countries. Moreover, various studies reveal that majority of patients with cervical cancer are from the developing countries probably due to absence of an efficient cancer screening system. It is therefore important to identify scenario of epithelial cell abnormality.[6,7] By the use of revised Bethesda system, various aspects of Pap smear interpretation have been clarified like adequacy, categorization, interpretation and results. Hence, using the Bethesda system, we have undertaken the study in Pap smear of women visiting the Gynaecology outpatient department in Lumbini Medical College Teaching Hospital(LMCTH), Palpa.

METHODS:

This study was carried out in the department of pathology, LMCTH. A cross-sectional study was carried out from March 2010 to October 2012. Significant history was carried out (parity, menstrual history) and findings of per vaginal examination (discharge, healthy/ unhealthy cervix) noted. Cervical smear was collected with the help of Ayre spatula, immediately fixed in alcohol for minimum of 30 minutes followed by pap staining, microscopy and interpretation. A total 1066 cases were studied. All unsatisfactory smears were asked for a repeat. Reporting and adequacy was assessed according to revised 2001 Bethesda System.

RESULTS:

Out of 1066 pap smears, 71 (6.6%) showed cervical epithelial cell abnormality. The most frequent epithelial cell abnormality was LSIL. Other patterns were as shown in Table 1.

The mean parity was 3.43 and the majority of patients had parity more than three. Most of the epithelial cell abnormality was found between 18 to 30 years of age and predominantly were LSIL (Table 2). The most frequent finding in our study was HSIL and squamous cell carcinoma (in the biopsy examined). Overall age of incidence was reproductive age, with peak in the 33-40 years, mean being 39.73 years. Our study also showed wide age range (20-60 years). Most of the patients were married under 19 years of age as shown in Table 3.

Per vaginal discharge were the major findings of the patients, cervical erosion and nabothian cyst in decreasing order of frequency as shown in Table 4.

Table 1: Different categories of diagnosis in Pap smear (N=1066)

Pap result	n	%
NSIS 995 93.3	995	93.3
ASC-US 5 0.46	5	0.46
LSIL 49 4.59	49	4.59
HSIL 13 1.21	13	1.21
SCC	4	0.37

Table 2: Epithelial cell abnormality in Pap smear in different age groups

Age (yrs)	ASCUS	LSIL	HSIL	SCC
<18	0	0	0	0
18-22	2	20	1	0
23-29	2	22	2	0
>30	1	7	9	4
Total	**5**	**49**	**13**	**4**

Table 3: Age at first marriage of the patient with abnormal Pap smear

Age (yrs)	ASCUS	LSIL	HSIL	SCC
<15	0	1	1	1
15-19	2	19	7	2
20-24	2	18	4	1
25-29	1	10	1	0
>30	0	1	0	0
Total	**5**	**49**	**47**	**4**

Table 4: Findings of patients with abnormal Pap smear

	ASCUS	LSIL	HSIL	SCC
Erosion	2	12	8	0
Nabothian cyst	3	10	2	0
Discharge	0	27	3	0
Growth	0	0	0	4

DISCUSSION:

To some extent, our study provides overall picture of epithelial cell abnormalities in the Pap smear cytology of women attending this hospital in developing country. It is evident that unlike in the developed countries, Pap smear screening is not well organized. Most patients with abnormal cytology detected by screening process are the symptomatic ones presenting either with growth, erosion, discharge etc. Pap smear in these cases is done as a part of investigation for the management of patients. This signifies that cervical cancer screening is based only on clinical impression which is quite unpredictable in relation to cytologic screening. Therefore, facilities for Pap screening should be extended up to primary health care level. Other studies on the prevalence of cervical epithelial cell abnormality revealed 4.3% in a tertiary hospital in Kuwait, 5% in a referral hospital in Saudi Arabia, 0.95% in Jewish Israeli women, 1.66% in the western region of Saudi Arabia and 7.9% in south western Saudi Arabia.[8-10] Our studies revealed increased prevalence (6.6%) possibly because women visiting tertiary hospital only when they have specific complaints such as something coming out per vaginum, lower abdomen pain or discharge. It is obvious that they had come to visit hospital when the dyskaryotic cells in the cervical epithelium had already occurred.

Eldman et al. studied Pap smear from 29295 patients over a period of one year and abnormalities were as follows: 9.9% ASC-US, 2.5% LSIL, 0.6% HSIL, and 0.2% invasive cancer. They also showed that adolescent with an age range of 13-22 had a significantly higher rate of LSIL.[11,12] Another study in Brazil, where 1822441 Pap smears were examined over a period of five years, showed that low grade lesions were common at 15-30 years. Patients older than 40 years had the greatest incidence of invasive cancer. In comparison to previous studies, our study revealed the following scenario: 0.46% ASCUS, 4.59% LSIL, 1.21% HSIL and 0.37% squamous cell carcinoma.[13] Unfortunately, only a few percentage (12.2%) of women had undergone biopsy and histopathological examination.

Significant discrepancies were found between our study and the previous studies from other countries: the lower rate of ASC-US and higher rate of LSIL, probably due to lack of routine Pap smear screening and presentation with an advanced form. Drop out of some cases to private clinics could also be possible significant variation of ASC-US and LSIL. Moreover, as described in the revised Bethesda system, criteria for ASC-US might differ subtly among laboratories. Most of the patients in our study were married women when they were in there teens and these patients had increased risk of HPV infection as predisposition of the immature cervix of the adolescent to persistent HPV infection, which could develop cancer. Therefore, another strategy should also be oriented in sex education, family planning and if possible HPV vaccination.

CONCLUSIONS:

Our study highlights that patients above 40 years are at risk of premalignant as well as malignant lesions and no specific finding of premalignant lesion is present on visual inspection of cervix. Hence, women should properly go to screening program as per recommendation.

REFERENCES:

1. Toews HA. The abnormal Pap smear: A rationale for follow up. Can Fam Physician 1983; 29: 759-62.

2. Elmslie TJ. The pap smear and cervical cancer screening. Can Fam Physician 1987; 33: 131-7.

3. Adhikari AK, Banik U, Numaga J, Suzuki E, Inada T, Okabe N. Heterogeneity of the fi bre sequence in subgenus C adenoviruses. J Clin Pathol 2004; 57:612-7.

4. Chhieng DC, Roberson J, Gidley J. Bethesda 2001. Impact on the reporting of gynaecologic cytology. Acta Cyto 2004; 48:355-62.

5. Solomon D, Schiff man M. ASCUS LSIL Triage study group. Qualification of ASCUS. Acomparision of equivocal HSIL in cervical cytology in the ASCUS LSIL Triage study. Am J Clin Pathol 2001; 116:386-94.

6. Jamal AA, Al-Maghrabi JA. Profi le of Pap smear cytology in the western region of Saudi Arabia. Saudi Med J 2003; 24:1225-9.

7. Cho H, Kim JH. Treatment of the patients with abnormal cervical cytology: A "See-and-treat" versus three-step strategy. J Gynecol Oncol 2009; 20:164-8.

8. Kapila K, George SS et al. Changing spectrum of squamous cell abnormalities observed in Mubarak Al-kabeer Hospital, Kuwait, over a 13-years period. Med Pnic Pract 2006; 15:253-9.

9. Abdullah LS. Pattern of abnormal Pap smear in developing countries: A report from a large referral hospital in Saudi Arabia using a 2001 Bethesda System; Ann Saudi Med 2007; 27:268-72.

10. Sadan O, Schejter E et al. Premalignant lesions of the uterine cervix in large cohort of Israeli Jewish women. Arch Gynecol Obstet 2004; 269:188-91.

11. Edelman HA, Fox A. Cervical Pap smear abnormalities in inner Bronx adolescents: Prevalence, Progression, and immune modifiers. Cancer Cytopathol 1999; 110:123-7.

12. Bishop A, Wells E. Cervical cancer: Evolving prevention strategies for developing countries. Reprod Health Matters 1995; 6:60-71.

13. Wang PD, Lin RS. Sociodemographic factors of Pap smear screening in Taiwan. Taipei Wanhawa district centre, Taiwan. Public Health 1996; 110:123-7.