Original Article

Correlation of PAP smear findings with clinical findings and cervical biopsy

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Abstract

Objectives: Carcinoma of the cervix is the most common cause of the death in Nepal. Cervical carcinoma does not develop suddenly from normal epithelium but is presented by a spectrum of intraepithelial neoplastic changes that are precancerous lesion and were termed as cervical intraepithelial neoplasia (CIN). Cervical cytological screening is designed to detect over 90% of cytological abnormalities. It has also been established that most cervical cancers can be diagnosed at the preinvasive stage with adequate and repetitive cytological screening. Keeping in view of the importance of carcinoma and the precancerous lesion (CIN) of cervix, study of different methods for the early detection of abnormalities in cervix, correlation with the clinical findings and comparison between the techniques was carried out.

Material and methods: Patients with suspicious cervix attending Gynaecology OPD of TUTH and Western regional hospital (Pokhara) who have undergone for pap smear cytology test along with biopsy were selected. Detail history with clinical examination was performed and the findings were correlated.

Results and conclusion: Unhealthy cervix with discharge was found to be common even in chronic cervicitis however bleeding and tenderness were associated with more advanced lesions. Pap smear test was found to be equally sensitive to histopathological examination for the early detection of different cervical lesions. However, it is advised to perform biopsy if any abnormalities are detected in pap smear for correlation and confirmation.

Key words: Pap smear, CIN

Carcinoma of the cervix is the most common cause of the death in Nepal. In a study carried out in the Teaching Hospital in the year 1998, 9.76% of all cancers were carcinoma cervix the third most common of all cancers. Mortality due to carcinoma of the cervix world wide is 195,000 numbers of deaths per year. Incidence of the carcinoma cervix in the developed world is 90,000 numbers of the cases and in the developing world is 340,000 numbers of cases[1]. Almost 50% of the death from cervical carcinoma occurs in the two decades of life from 45 to 65 years with a range from 20 to over 85 years. It has been estimated that an average women under 40 years of age has a 2% chance of developing cervical carcinoma [2]. Subsequent studies showed that cervical carcinoma does not develop suddenly from normal epithelium but is presented by a spectrum of intraepithelial neoplastic changes which are precancerous lesion and were termed as cervical intraepithelial neoplasia (CIN).[3, 4, 5] Several reports stated that if these lesions were untreated, up to one-third of these precancerous cases developed in carcinoma.[6, 7]

The concept of preinvasive disease of the cervix was first introduced by Papanicolaou in 1947 and since then, cervical cytological testing has become the standard screening test for cervical neoplasm. [8] Cervical cytological screening is designed to detect over 90% of cytological abnormalities[6].

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It has also been established that most cervical cancers can be diagnosed at the preinvasive stage with adequate and repetitive cervical cytological screening. Thus it is felt that an organized screening programme, aimed at the entire female population, should significantly reduce the mortality. Treatment of precancerous lesion is simple, safe, very often non-destructive and usually curative.[9]

CIN is defined as a spectrum of intraepithelial cellular atypia of mild degree at the base of the cervical squamous epithelium or squamous like metaplastic columnar epithelium of cervix to severe degree involving the full thickness of the epithelial lining [3].

The original terminology of dysplasia and carcinoma in situ (WHO) classification was replaced by the cervical intraepithelial neoplasia (CIN terminology) proposed by Richart, [5] in order to emphasise a continuum of disease. Recently the Bethesda system of terminology has been introduced to sub-classify the lesions into grades: high grade and low grade Squamous Intraepithelial Lesions (SIL). [10] The terminologies are compared in the table below:

Keeping in view of the importance of carcinoma and the precancerous lesion (CIN) of cervix, study of different methods for the early detection of abnormalities in cervix and comparison between the techniques was carried out.

WHO system (Dysplasia terminology)	CIN terminology	Bethesda terminology
Mild dysplasia	CIN I	Low grade SIL
Moderate dysplasia	CIN II	High grade SIL
Severe dysplasia	CIN III	High grade SIL
Carcinoma in situ	CIN III	High grade SIL

Aims and objectives
General
    To correlate between Pap smear cytology and cervical biopsy with clinical findings
Specific
    To correlate the Pap smear cytology with histological reports
    To correlate the Pap smear cytology with clinical findings

Inclusion criteria
All of the patients with suspicious cervix having abnormality either in pap smear or in biopsy
Symptomatic patients with normal cervix having abnormality either in pap smear or in biopsy.

Exclusion criteria
Clinically asymptomatic with normal cervix
Suspicious cervix within normal Pap smear or biopsy reports

Materials and methods
All the patients with suspicious cervix attending Gynaecology OPD of TUTH and Western Regional Hospital (Pokhara), who have undergone for pap smear cytology test along with biopsy, were selected. Detail history with clinical examination is performed and the findings were correlated.

Results
15% of the cases were found to have malignancy and seen even in younger age group 21-30 years however it was found to be less common among the age group of >71 . It could be due to the higher screening modalities.

P/V discharge is found to be the commonest complaints in different lesions of the cervix however p/v bleeding is found to be more specific for cervical malignancy.

Unhealthy cervix with discharge was found to be common even in chronic cervicitis however bleeding and tenderness are associated with more advance lesions.

Unhealthy cervix with PV bleeding and discharge are found to be more common in advance lesions

however tenderness is found to be associated with malignancy.

Considering the histopathology reports as the gold standard, pap smear test is also found to be equally sensitive. But it is advised to perform biopsy if any abnormalities are detected in pap smear because technical errors like sampling error was found to be the number one cause of false negative reports. This can be overcome by following strictly the instructions of technique of pap smear and performing biopsy if any abnormalities are detected in pap smear.

Table 1: Prevalence of abnormal cervical smears in different age group

Age Group (years)	Diagnosis						
	Chronic Cervicitis	Mild Dysplasia	Moderate Dysplasia	Severe Dysplasia	Ca. in Situ	Malignancy	Total
21-30		7	2		1	1	11
31-40	1	6	1	1		2	11
41-50	1	5	3	2		2	13
51-60	1			1			2
61-70						1	1
>71		1		1			2
Total	**3**	**19**	**6**	**5**	**1**	**6**	**40**

Table 2: Correlation between clinical findings with various lesions of the cervix

Signs/ Symptoms	Chronic Cervicitis	Mild Dysplasia	Moderate Dysplasia	Severe Dysplasia	Ca. in Situ	Malignancy
Pain	33.33%	100%	83.33%	80%	100%	66.66%
P/V Discharge	100%	100%	100%	80%	100%	100%
P/V Bleeding		26.3%	50%	60%		100%
Wt. loss	33.3%	15.79%	33.33%	60%	100%	66.66%
Dysuria	33.33%	52.6%	50%	80%	100%	66.66%

Table 3: Correlation of pap smear findings with clinical finding

Diagnosis	Clinical Findings			
	Tenderness	PV Bleeding	Discharge	Unhealthy Cervix
Chronic Cervicitis	0/15	3/15	15/15	15/15
Mild Dysplasia	2/12	7/12	9/12	11/12
Moderate Dysplasia	2/3	3/3	3/3	3/3
Severe Dysplasia	4/7	6/7	7/7	7/7
Malignancy	3/3	3/3	3/3	3/3

Table 4: Correlation between histopathological findings with clinical findings

Diagnosis	Clinical Findings			
	Tenderness	PV Bleeding	Discharge	Unhealthy Cervix
Chronic Cervicitis	-	-	33.33%	66.66%
Mild Dysplasia	5.26%	26.32%	95%	100%
Moderate Dysplasia	16.67%	83.33%	100%	100%
Severe Dysplasia	40%	100%	100%	100%
Ca. in situ	100%	100%	100%	100%
Malignancy	100%	100%	100%	100%

Table 5: Comparison of PAP smear with biopsy reports

Diagnosis	Pap smear	Biopsy report	
Chronic Cervicitis	**15**	Mild dysplasia-	14
		Moderate Dysplasia-	1
Mild Dysplasia	**12**	Ch. Cervicitis-	2
		Mild dysplasia-	4
		Moderate dysplasia-	4
		Severe Dysplasia-	2
Moderate Dysplasia	**3**	Mild dysplasia-	1
		Malignancy-	2
Severe Dysplasia	**7**	Ch. Cervicitis-	1
		Severe dysplasia-	2
		Ca in situ-	1
		Malignancy-	3
Ca. in situ			
Malignancy	**3**	moderate dysplasia-	1
		Severe dysplasia-	1
		Malignancy-	1
Total	**40**		**40**

Table 6: Comparison of biopsy with PAP smear reports

Diagnosis	Biopsy	Pap smear report	
Chronic Cervicitis	3	Mild dysplasia-	2
		Severe dysplasia-	1
Mild Dysplasia	19	Ch. Cervicitis-	4
		Mild dysplasia-	14
		Moderate Dysplasia-	1
Moderate Dysplasia	6	Ch. Cervicitis-	1
		Mild dysplasia-	4
		Malignancy-	1
Severe Dysplasia	5	Mild dysplasia-	2
		Severe dysplasia-	2
		Malignancy-	1
Ca. in situ	1	Severe dysplasia	1
Malignancy	6	moderate dysplasia-	2
		Severe Dysplasia-	3
		Malignancy-	1
Total	**40**	**40**	

Discussion

Carcinoma of the cervix is the most common frequent of all the genital cancers and after the breast, the second most common site of malignancy in the female body. In a study carried out in the Teaching Hospital in the year 1998, 9.76% of all cancers were carcinoma cervix, the third most common of all cancers [1].

Mortality due to the carcinoma of the cervix world wide is 195,000 numbers of deaths per year. Prevalence of the carcinoma cervix worldwide is 3,955,000 numbers of cases [1]. It has been estimated that that an average women under 40 years of age has 2% chance of developing cervical cancer [2]. Subsequent studies showed that cervical carcinoma does not develop suddenly from normal epithelium but is presented by a spectrum of intraepithelial changes which are precancerous lesion and were termed as CIN. [3, 4, 5] If these lesions were untreated, up to 1/3 of these precancerous cases develop in carcinoma. [6, 7]

As the cervix is relatively easily accessible organ, the logistics for screening cervical cancer are also simple. Screening programmes have reduced the incidence and mortality from cancer cervix in many developed countries. It is well accepted that pap smear has been the most effective cancer screening test ever introduced. This screening test has achieved a reduction in the death rate of more than 70% for a prevalent cancer. [11]

To date the cervical cancer prevention effort worldwide have focused on screening sexually active women using cytology smear and treating precancerous lesion thus by decreasing the incidence and mortality from cervical cancer. The diagnosis is made by screening an asymptomatic population, the test in use are cervical cytology, and histological examination of the biopsy material added by numerous technique such as Cervicography and assessment of HPV DNA type. In most developed countries, women are advised to have their first test soon after becoming sexually active and subsequently

every 1-5 years. The current recommendation of the American Cancer Society, National Cancer Institute, American College of Obstetrics & Gynaecologists and others [12, 13] is that all women who are sexually active above the age of 18 years should have annual pap smear for 3 years. If the women have 3 consecutive negative pap smear, the physicians may consider extending the interval of 3-5 years. The Canadian Task Force report (1976) recommended that sexually active women should have a cervical smear every 3 years after 2 negative smears. [14]

The abnormal smears were seen mainly among the age group 21-50 years which is sexually active age group. In a study done by Pradhan P[15], the abnormal smears were seen mainly among age group of 21-40 years and carcinoma was also found mainly among that age group. In our study carcinoma was found mainly among the age group of 21-50 years.

As per WHO 1996, 80% of cases present late in the incurable stage. Adenna & Okeke, 1995 reported that late presentation is related to the inherent shyness of the average women in the developing country in reporting or discussing matters related to the sex [16]. In our study, it was seen mainly in the zonal hospital and one carcinoma cervix was detected probably because of unawareness, negligence and shyness. However, abnormal smears were detected mainly in the Kathmandu Valley.

The most common presentation with cervical lesion in order of frequency are irregular vaginal bleeding, whitish discharge per vagina, bleeding/pain on coitus, cachexia, lower abdominal pain, dysuria. painful defecation and anorexia. In our study, P/V discharge was found to be the commonest complaints in different lesions of the cervix however pain and P/V bleeding were found to be more specific for cervical malignancy.

Bleeding and tenderness were the main signs that were found to be associated with more advance lesions however none of the signs were specific. Pradhan P [15] also found the similar findings.

Abnormalities either in pap smear or in biopsy reports were correlated with their corresponding biopsy and pap smears.

Some of the cervix which were diagnosed as severe dysplasia in pap smear were turned out to be malignancy which were confirmed by the biopsy. Even moderate dysplasia was turned out to be malignancy. Similarly, cases which were diagnosed as malignancy in pap smear were found to be only moderate dysplasia in biopsy.

Reports of cytology sensitivity in detecting cervical neoplasia ranged from 50%-98% [17]. Review of negative smear taken from patient who present with invasive cancer showed that sampling error and laboratory error are responsible in approximately equal numbers [18]. Many different approaches have been studying to improve the accuracy of cervical screening e.g. Colposcopy, cervicography etc.

Biopsy report is considered as the gold standard provided biopsy is taken from the appropriate site. In our study some of the case which was reported as malignancy in biopsy was reported to have moderate dysplasia in pap smear.

Pap smear test is found to be cheap, non-invasive and equally sensitive to biopsy however it is advised to perform biopsy if any abnormalities are detected in pap smear. Sampling error was found to be the number one cause of false negative report.

Conclusion
Carcinoma of the cervix is the most common cause of death in Nepal. Cervical carcinoma does not develop suddenly from normal epithelium but is presented by a spectrum of intraepithelial neoplastic changes which are precancerous lesions and were termed as cervical intraepithelial lesion.

Keeping in view of the importance of carcinoma and the precancerous lesion (CIN) of the cervix, study of different methods for the early detection of abnormalities in cervix, comparison between the technique and correlation of the abnormalities with the clinical findings was carried out. 40 patients with suspicious cervix attending Gynaecology OPD of TUTH and WRH (Pokhara), who have underwent for pap smear cytology test along with biopsy were selected. Detail study with clinical examination was performed and the findings were correlated.

Cervical intraepithelial lesion and malignancy were found to be common among the age group of 21-50 years however malignancy was found to be less among the older age group. Pain and P/V discharge were found to be the most common complaints among different lesions of the cervix however most of the signs and symptoms were not specific for malignancy. Unhealthy cervix with discharge was found even in chronic cervicitis however tenderness along with P/V bleeding were found to be associated with more advance lesions.

Some of the cervix which were diagnosed as severe dysplasia in pap smear were turned out to be malignancy in biopsy. Even moderate dysplasia was turned out to be malignancy. Similarly, cases which were diagnosed as malignancy in pap smear were found to be only moderate dysplasia in biopsy.

Pap smear test was found to be equally sensitive to histopathological examination for the early detection of different cervical lesions. However, it is advised to perform biopsy if any abnormalities are detected in pap smear for correlation and conformation.

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