

A Clinical Audit of Pap Smear Test for Screening of Cervical Cancer

Tamrakar SR, Chawla CD

Department of Obstetrics and Gynecology, Dhulikhel Hospital-Kathmandu University Hospital, Dhulikhel, Kavre

Aims: Cervical cancer is a major cause of morbidity and mortality in gynecology clients. It accounts for the most common cancer in women. A Papanicolaou (Pap) smear test (cervical cytology screening) is one of the best tests to screen for cervical cancer in its premalignant stage. The objective of this study is to find out the prevalence of abnormal Pap smear results and to determine the contributing factors for it.

Methods: The out patient clinic register was reviewed. Out-patients clinic register from 1 Jan 2008 to 31 Dec 2011 showed that a total of 25511 gynecology clients were seen. In these four years duration, a total of 1506 Pap smear samples were taken which accounted for 5.9% of the total gynecology clients. The samples were collected only after proper counseling and consent from the clients who visited the clinic for various gynecology complaints. Assumed predictors of abnormal Pap smear results were examined through inferential way (Chi square test) using Software SPSS version 13.0 for Windows.

Results: The preliminary analysis showed the mean age was 37.57 ± 10.72 years (ranging from 18 to 81 years). Most of them were of Newar caste (28.7%), with 3 children (37.6%) and from Kavre District (66%). Most of them (343 clients) were of age group 30 – 34 years whereas 15.8, 10.8, 3.1 and 10.0 % (clients were of 40 – 44, 45 – 49, 50 – 54 and 55 above respectively). A total of 1062 samples were normal whereas 379 samples were suggestive of inflammatory and 39 samples were inadequate for evaluation. We had 22 samples suspicious for malignancy and/or low grade squamous intraepithelial lesion (LSIL) and 4 frank malignant cases. This accounted for 1.7% of total Pap smear samples. These cases were scheduled for colposcopic guided biopsies and histologic evaluations. There was significant difference between the age groups and Pap smear results ($p=0.003$) and parity with Pap smear results ($p=0.000$, highly significant). But there was no significant difference between caste and Pap smear results ($p=0.166$).

Conclusions: There is no doubt that Pap test is one of the best and easiest tests to screen for precancerous and cancerous cervical lesions. In order to have a high yield it has to be combined with other alternative tests like HPV testing and/or visual inspection with acetic acid (VIA) or Lugol's Iodine (VILI). Besides its use as screening tool, we can also evaluate for chronic cervicitis, sexually transmitted infection (STI), pelvic inflammatory disease (PID) and genital prolapse (if any) in same setting. Thus the community people will have broader benefits from the screening program.

Keywords: Cervical cancer, HPV testing, Pap smear, VIA, VILI

INTRODUCTION

Cervical cancer is a major cause of morbidity and mortality in gynecology clients. It is the leading cancer among women in developing countries like Nepal. Evaluation of screening performance for effective, feasible and affordable early detection and management methods is a public health priority. Five screening methods, naked eye visual inspection of the cervix after application of diluted acetic acid (VIA), of Lugol's Iodine (VILI) or with a magnifying device (VIAM), the Pap smear and human papilloma virus (HPV) testing with high-risk probe of the

Hybrid Capture-2 assay (HC2) are being used to screen and detect the cervical cancer in precancerous stage.¹

Cytology is a simple and inexpensive diagnostic method and is therefore especially useful in areas with limited resources. Even though the Pap smear test alone does not have a high sensitivity and specificity, it is the most commonly used test in most screening programs.² This clinical audit was done to find out the prevalence of abnormal Pap smear results and the contributing factors for it.

CORRESPONDENCE

Dr Suman Raj Tamrakar, MD
Assistant Professor
Department of Obstetrics and Gynecology,
Dhulikhel Hospital-Kathmandu University Hospital,
Dhulikhel, Kavre
Phone: 9741121546
Email: drsuman537@yahoo.com

METHODS

The pap smear samples were collected after proper counseling and informed consent was taken from the clients visiting the clinic for various gynecology complaints. Assumed predictors of abnormal Pap smear results were examined through inferential way (Chi square test) using Software SPSS version 13.0 for Windows.

RESULTS

The out patient clinic register of Dhulikhel Hospital (DH) from 1 Jan 2008 to 31 Dec 2011 showed that a total of 25511 gynaecology clients had received services. In these four years duration, 1506 Pap smear samples were taken which account for 5.9% of these clients.

A total of 1062 samples were normal whereas 379 samples were suggestive of inflammatory and 39 samples were inadequate for evaluation. We have got 22 samples suspicious for malignancy and/or LSIL and 4 frank malignant cases. These account for 1.7% of total Pap smear samples. These cases were scheduled further for colposcopic guided biopsies and histologic evaluations.

There was significant difference in Pap smear result according to the age group (p=0.003) and parity (p=0.000, highly significant). But there was no significant difference in Pap smear result in different castes (p=0.166).

Table 1. Comparison of Pap Smear results according to age group

Papsmear	Normal	Inflamm	LSIL	Suspi	Inadequate	+ve for malig	Total
Age ≤24	87(77.0%)	22(19.5%)	1(0.9%)	1(0.9%)	2(1.8%)	0(0.0%)	113
25-29	155(74.2%)	52(24.9%)	0(0.0%)	0(0.0%)	2(1.0%)	0(0.0%)	209
30-34	229(66.8%)	101(29.4%)	0(0.0%)	1(0.3%)	11(3.2%)	1(0.3%)	343
35-39	181(73.9%)	56(22.9%)	1(0.4%)	2(0.8%)	5(2.0%)	0(0.0%)	245
40-44	175(73.5%)	49(20.6%)	1(0.4%)	3(1.3%)	10(4.2%)	0(0.0%)	238
45-49	115(71.0%)	40(24.7%)	1(0.6%)	2(1.2%)	3(1.9%)	1(0.6%)	162
50-54	32(69.6%)	12(26.1%)	1(2.25%)	1(2.2%)	0(0.0%)	0(0.0%)	46
≥55	88(58.7%)	47(31.3%)	0(0.0%)	7(4.7%)	6(4.0%)	2(1.3%)	150
Total	1062	379	5	17	39	4	1506

Table 2. Comparison Pap Smear results according to parity

Papsmear	Normal	Inflamm	LSIL	Suspi	Inadequate	+ve for malig	Total
Parity 0	13(92.9%)	0(0.0%)	0(0.0%)	0(0.0%)	1(7.1%)	0(0.0%)	14
1	100(75.8%)	30(22.7%)	0(0.0%)	1(0.8%)	1(0.8%)	0(0.0%)	132
2	353(72.8%)	121(24.9%)	1(0.2%)	1(0.2%)	9(1.9%)	0(0.0%)	485
3	401(70.8%)	139(24.6%)	1(0.2%)	5(0.9%)	18(3.2%)	2(0.4%)	566
4	117(67.2%)	47(27.0%)	2(1.1%)	2(1.1%)	6(3.4%)	0(0.0%)	174
5	78(57.8%)	42(31.1%)	1(0.7%)	8(5.9%)	4(3.0%)	2(1.5%)	135
Total	1062	379	5	17	39	4	1506

Table 3. Comparison of current study with previous clinical studies

Author	Sample Size	Results
Sherpa et al ⁶ (2009)	n=932	3.6% abnormal pap smear
Dharbhadel et al ⁷ (2004)	n=350	0.57% positive pap smear
Pradhan ⁸ (2002)	n=800	4.8% abnormal pap smear
Sarian et al ⁹ (2005)	n=11834	2.2% (LSIL threshold) 1.1% (HSIL threshold)
Sankaranarayanan et al ¹⁰ (2003)	n=4444	3.4%
Current Study	n=1506	1.7% premalignant and malignant

DISCUSSION

Gynecological cancers are among the preventive cancers. Cervical cancer is the most common female genital tract malignancy among Nepalese women. Cervical cancer can be prevented and premalignant conditions can be detected before invasion by different tests.³

It was recommended that women who are negative on both tests (cytology and HPV DNA testing) do not require rescreening for 3 years. It is well established that on average it takes approximately 10 years for a CIN 2,3 lesion to progress to an invasive cancer (i.e. the transit time).⁴

No population-based estimates of cervical cancer incidence in Nepal exist, but WHO has estimated that the incidence rate is approximately 26-28 per 100 000 women per year. Though the prevalence of cervical cancer in Nepal is not well documented, it is the most commonly reported malignancy among women in Nepal with approximately 2150 invasive cervical cancers and 1100 deaths annually.⁵

In developed countries, initiation and sustainability of cervical cytology programs involving the screening of sexually active women annually, or once in every 2-5 years, have resulted in a large decline (up to 80%) in cervical cancer incidence and mortality over the last 40-50 years.^{11,12}

The WHO recommends that in developing countries, women aged 18-69 years should be screened for cervical cancer every 3 years. In Nepal only 2.4% of women in this category currently meet this standard.¹³ There was significant difference in Pap smear results between different age group ($p=0.003$). As the age of the clients advances, LSIL, suspicious lesions and frankly malignant cases were seen more. For example in the age group ≥ 55 years seven suspected lesions and two malignant cases were seen.

Epidemiological studies conducted during the last 40 years have consistently indicated that cervical cancer risk is strongly influenced by measures of sexual activity: number of sexual partners, age of first intercourse and sexual behavior of the woman's male partners.^{14,15}

History of sexually transmitted diseases increases the risk of developing cervical cancer. Tobacco smoking is a well-known risk factor for cervical cancer.¹⁶ A direct carcinogenic action of cigarette smoking on the cervix has been proposed since nicotine metabolites can be found in the cervical mucus of women who smoke.

Though smoking habit of the clients was not assessed in this study, smoking habit in female populations in Nepal was quite common. The number of live births is a consistent risk factor for cervical cancer. Previous studies done by Brinton have shown that there is a linear trend in the association between parity and risk.¹⁷ In this study, there was significant difference between parity with abnormal pap smear result ($p=0.000$, highly significant). As the parity of the clients advances, LSIL, suspected lesions and positive for malignant cases were seen more. Notably more LSIL, suspected lesions and malignant cases were seen in para ≥ 3 .¹

Among the general population, the overall prevalence of HPV was 8.6% (6.1% for high-risk types). Approximately 80% of cervical cancer in Nepal is theoretically preventable by HPV 16/18 vaccines.⁶ Though many of the studies included in one meta-analysis are quite old and were conducted before the introduction of liquid-based cytology

or the use of cyto-brushes, the meta-analysis (which reviewed 94 screening studies) found that the sensitivity of cervical cytology ranged from 30% to 87%.²

The cytology result allows HPV DNA positive women to be triaged into 2 groups, those requiring colposcopy and those who can simply be followed-up. Liquid based cytology enables the use of supplementary methods in the diagnosis and prognosis of cervical lesions.¹⁸ Liquid based cytology was significantly more sensitive than conventional cervical cytology for detecting CIN 2.⁴

A prospective study ($n=350$) conducted by Dhaubhadel et al found that VIA as a screening test for cervical neoplasia did not miss any lesion detected by Pap smear and confirmed by cervical biopsy.⁷

Qureshi et al evaluated the effectiveness of VIA and VILI compared to Pap smear as screening methods for carcinoma of the cervix, the results were as follows: Pap smear test (sensitivity 20.83%, specificity 98.38%), VIA (55.5%, 71.39%), and VILI (86.84%, 48.93%). They concluded that VIA and VILI are less specific in comparison to the Pap smear but they are more sensitive in detecting pre-invasive lesions. Hence VIA and VILI can be used as cervical cancer screening tools in low-resource settings.^{10,19}

However, the Latin American screening (LAMS) study ($n=11834$) failed to reproduce the performance figures obtained with VIA and VILI (as stand-alone tests) in some other settings, where the prevalence of cervical disease was higher. A combined use of VIA or VILI with the Pap test or HC2 allowed specific detection of cervical abnormalities.⁹ The largest ever study ($n=58000$) in the developing countries performed by Arbyn et al found VIA had a sensitivity of 79% and 83%, and a specificity of 85% and 84% for the outcomes CIN2 and CIN 3, respectively. VILI was on average 10% more sensitive and equally specific. VIA showed similar results as VIA. The pap smear showed lowest sensitivity. The HC2-assay showed sensitivity for CIN2 of 62% and a specificity of 94%. Results of visual tests and colposcopy were highly correlated.¹

In another study, most of the high-risk HPV DNA positive women who subsequently developed biopsy-confirmed CIN 3 were infected with HPV 16 or HPV 18.²⁰ Hence women with specific high-risk types of HPV such as HPV 16, 18, 33, 45 or 31 (the 5 most common HPV types found in cervical cancers) would be referred to colposcopy whereas those with other high-risk types of HPV would be followed-up in 12 months with a repeat HPV DNA test.⁴

More recent research studies continue to report that the sensitivity of a single cervical cytology test is relatively low hence an alternative strategy that appears even more promising to screen using HPV DNA testing alone and use a combination of both reflex cytology and HPV genotyping.⁴

CONCLUSIONS

Cervical cancer is a relatively neglected disease in terms of advocacy, screening and prevention from professional or public health organizations. There is no doubt that Pap test is one of the best and easiest tests to detect precancerous cervical lesions. In order to have a high yield it has to be combined with other alternative tests like HPV testing and/or visual screening with acetic acid (VIA) or Lugol's Iodine (VILI).

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