Value of Conventional cervical cytology as a screening test for cervical cancer

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ABSTRACT

This is a prospective study conducted in the department of Obstetrics and Gynecology of Nepal Medical College Teaching Hospital, Kathmandu, Nepal. The main Objective of the study is to see the value of opportunistic screening program for cervical pre-cancerous lesion for prevention of cervical cancer. It also aims to see how many cases can be picked up by such screening test and is it worth doing this tset? We analysed 1751 cases of pap smear taken during almost 2 years period and found inflammatory smear being the predominant finding and it was found in reproductive age group. We had 1.14% cases of abnormal smear and 0.74% cases were proved by biopsy.

Keywords: Pap smear, pre-cancerous lesion, carcinoma cervix

INTRODUCTION

Cervical cancer is the second most common cancer in women worldwide.[1] it is the most common cancer of women in developing countries, where it is estimated that only about 5% of women have been screened for the disease with pap smear, compared to 40-50% in developed countries.[2] Unlike most other canc ers, cervical cancer is readily preventable when effective programs are conducted to detect and treat its precursor lesions. The easy accessibility of the cervix and the propensity of the cancer cells to exfoliate from its surface have enabled us to study the process of malignant transformation in the cervix in very early stage.[4] Because of poor access to screening and treatment services, the vast majority of deaths still occur in women living in low- and middle-income countries. Cervical cytology screening is helping to reduce cervical cancer rate dramatically since its implementation from 1950s.[4,5] Effective methods for early detection of precancerous lesions using cytology (Pap smear) exist and have been shown to be successful in high income countries. However, competing health care priorities, insufficient financial resources, weak health systems, and limited numbers of trained providers have made high coverage for cervical cancer screening in most low- and middle-income countries difficult to achieve. Every year more than 270 000 women die from cervical cancer, more than 85% of these deaths are in low and middle income countries.[2]

Cervical cancer is caused by sexually-acquired infection with Human papillomavirus (HPV). Most people are infected with HPV shortly after onset of sexual activity, which is the most common viral infection of the reproductive tract. Almost all sexually active will be infected with HPV at some point in their lives and some may be repeatedly infected. The peak time for infection is shortly after becoming sexually active. The majority of HPV infections resolve spontaneously and do not cause symptoms or disease. However, persistent infection with specific types of HPV (most frequently, types 16 and 18) may lead to precancerous lesions. If untreated, these lesions may progress to cervical cancer.[5]

The increasing availability of an alternative screening technology called VIA (visual inspection with acetic acid), VILLI (visual inspection with lugol iodine) and new vaccines against the Human papillomavirus (HPV) may help to prevent cervical cancer further. Moreover, because HPV vaccination targets 9–13 year old girls, there is the opportunity to catalyse a life course approach to cervical cancer prevention and control from childhood and through adulthood.[6] Cervical cancer screening is the systematic application of a test to identify cervical cellular abnormalities in an asymptomatic population. Women targeted for screening may actually feel perfectly healthy and see no reason to visit health facilities.[1-4] Screening services may be provided either as an opportunistic (i.e. taking advantage of a woman's visit to the health facility for another purpose), organized services or a combination of both. It is generally accepted that organized screening is more cost-effective than opportunistic screening, making better use of available resources and ensuring that the greatest number of women will benefit.

Three different types of tests are currently available:1

- Conventional (Pap) and liquid based cytology (LBC)
- Visual inspection with Acetic Acid (VIA) and VILLI (visual inspection with lugol's iodine)

- HPV testing for high risk HPV types (e.g. types 16 and 18).

HPV vaccination does not replace cervical cancer screening. In countries where HPV vaccine is introduced, screening program may need to be developed or strengthened.

Conventional pap smear is simply examination of exfoliated cells in cervical scraping taken with ayer's spatula and endocervical brush, Slide are prepared and examined under microscope for it's cellular architecture, nuclear pattern and cytoplasm nuclear ratio. Degree of cellular differentiation is classified according to Bethesda system.

Visual inspection with acetic acid (VIA) involves swabbing the cervix with a three- to five-percent acetic acid (vinegar) solution before visual examination with a strong light source. The application of acetic acid causes precancerous lesions to temporarily turn white, allowing the health care provider to determine whether precancerous lesions are present.

Visual inspection with Lugol's iodine (VILI)- also known as "Schiller's test," uses Lugol's iodine instead of acetic acid to identify potential precancerous lesions. The screening test is similar in approach to the Schiller's iodine test advocated in the 1930s and widely used early in the twentieth century, before the development of cytology. The application of iodine to the cervix results in a brown or black stain on areas that contain glycogen. Because precancerous lesions and invasive cancer do not contain glycogen, they do not take up the iodine, and therefore appear as well-defined, thick, mustard-colored or saffron-yellow areas. VILI may have better test performance characteristics than VIIA.

There is growing interest among cervical cancer prevention researchers in HPV DNA testing as a primary screening test. HPV DNA testing identifies high-risk HPV DNA subtypes. The presence of high-risk HPV strains indicates that a woman has an increased risk of developing cervical cancer. When used in women in their thirties and forties, HPV DNA testing is objective and generally has a higher sensitivity and specificity for detecting high-grade cervical lesions than does visual screening.

Sensitivity levels for HSIL have been found to range from 84 to 97 percent; specificity has been found to be approximately 90 percent. Screening programs based on HPV DNA testing could give women the option of using self-collected sampling techniques, although this approach has not yet been broadly tested. Self-collection of vaginal samples could significantly reduce the number of trained medical personnel needed to implement the screening program, because vaginal examinations only would be required for the fraction of screened women who are HPV positive.

women younger than 30 years of age need not undergo HPV DNA screening except for women known to be HIV-infected or living in a high HIV prevalence area.

OBJECTIVE

The objective of the study is to analyse the results of pap smear taken in NMCTH.

To see the ability of opportunistic pap smear to pick up abnormal smear.

MATERIALS AND METHODS

The present study is a prospective study conducted in the department of Obstetrics and Gynecology of Nepal Medical College Teaching Hospital. Kathmandu, Nepal. Basically it was an opportunistic screening where patients visiting hospital for one or other reason were included in the study. It was started from 1st of January 2010 and was continued till December 2012. All consecutive female were included in the study if they were agreed for the test. All women were explained about the importance of pap smear and it's role for preventing cervical cancer.

Detail history and clinical findings were recorded and Pap smear was taken. All of them were told to bring the report of smear to the department and according to the reports treatment was provided. Inadequate sample, Severe infection or bloody sample which makes difficult to comment on cellular pattern were excluded from study. As our pathologists follow the Bethesda system to write the reports of pap smear, we tabulated accordingly. The reports were generally classified as normal, inflammatory, ASCUS, LSIL, HSIL and in situ. Data were collected from pathology department as well as from operation theatre to tally the reports and to confirm the diagnosis in cases of abnormal reports. Data were tabulated and analysed simply.

DISCUSSION

Screening for any disease aims to detect the disease in it's earlist possible stage and treat it so that it prevents the morbidity and mortality due to it's advanced stage which also decreases the economic burden to the person, family as well as to the country. Cervical cancer is the most commonly screened disease in female and if it is carried out effectively, it significantly decreases the death due to it.

There are a lot of research on screening of cervical precancerous lesion world wide with the aim to

reduce the death of women due to cervical cancer. In Nepal also many papers are published but overall prevalence is not exactly known. Various studies are carried out in different region, some of them are organized screening program me and some are opportunistic screening program. The incidence depends on the type of screening program. The result of organized screening (where everyone will be screened) can not be compared with opportunistic screening where women come for check up with some gynecological problem. Although one-third of the world cervical cancer burden is endured in India, Bangladesh, Nepal and Sri Lanka, there are important gaps in our knowledge of the distribution and determinants of the disease in addition to inadequate investments in screening, diagnosis and treatment in these countries.[7]

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 reported and 1100 deaths annually.[8]

A large study conducted in only one full fledge cancer hospital in Nepal over 10 years period from 1999 till 2008 showed total of 11469 cases of all cancer with 3372 cases(29%) of cervical cancer . Total number of cases showed a rising pattern over the ten year period. This is in sharp contrast to the US and other western countries where there has been decreasing trend over the past few years .It demands for dare need of organized screening program for cervical carcinoma.[9] Data from studies in developing countries such as Western Cape, South Africa suggest that even limited Pap smear screening reduces the risk of cervical cancer.[10]

Comparison of studies done in the same Hospital (NMCTH)

Year	no.of cases	Abnormal smear	References
2003	100	3%	11
2008	800	4.8%	P. Pradhan12
2010	1751	1.14%	present study

This variation is probably due to the fact that during initial days after establishment of the Hospital, we used to take the smear only in selected cases (the cervix looks abnormal and need to be screened). For the last few years we take pap smear routinely in all female visiting Gynecological out patient departments if they have no smear in the last one year. Incidence also depends on sample size.

COMPARISON OF DIFFERENT STUDIES DONE IN DIFFERENT PARTS OF NEPAL

References	Year	no.of cases	Abnormal smear
Sherpa et al13	2009	n=932	3.6% abnormal pap smear
Dharbhadel et al14	2004	n=350	0.57% positive pap smear
Sankaranarayanan et al[15]	2003	n=4444	3.4% Abnormal sample
K Vadehra16	2006	n=500	5.5% abnormal smear
Tamrakar S[8]	2012	n=1506	1.7% abnormal smear
Vaidya A17	2003	n= 200	9% - high risk,3%- non high risk
Ranabhat SK18	2011	n= 880	abnormal smear 1.7%
Present study	2010	n= 1751	1.14% abnormal smear

While comparing the results of some of the studies carried out in south Asial countries, we get a lot of variation in the results, it all depend on the type of screening and trained personnel involved in the procedure.

A study done in India by Tiwari et al in 100 cases, 5% were abnormal smear with equal number of CIN I and CIN II.[19] Similar result was found by Neelima and colleague with 80% inflammatory and 9.5% epithelial abnormality.[20] Similar study done in Maharastra, India by Dhiraj et al showed 5.8% of study population to be abnormal or precursor of cervical malignancy.[21] As cervical cancer is more common in women with multiple sex patrnes and may be associated with other STDs including AIDS. A study done in Panjab, India in STD clinic with 300 cases of pap smear ,the incidence of abnormal epithelial smear was in 3.6%.[22] All of these results showed higher incidence of abnormal smear than our study.

In Pakistan-Rubina et al studied pap smear of 500 cases, 55.6% the smear was reported negative for malignancy, 36.4% had an inflammatory smear, 6% had CIN and in 2% the smear was inadequate for cytological examination.[23] Another study in Pakistan by Sonia et al in 300 cases found abnormal smear in 2.6% cases.[24] A large study conducted in Karachi,Pakistan over 7 years period in 20995 smear in a muslim population showed 0.55 abnormal smear ,34% inflammatory and 3.8% normal smear and remaining others.[25] This is too low in comparison with our study.

A study done in a Medical college of Bangladesh in 550

cases of pap smear and positive results were confirmed with biopsy, they had 15% abnormal smear of various degrees of epithelial abnormalities .[26] Another study carried out in a large group in the same country by Banik and colegues with 1699 pap smear, they found 8.18 % abnormal epithelial lesion.[27] Another small study done by jahanara B in 100 cases showed 1% abnormal epithelial abnormality.[28] So collectively the incidence of abnormal smear in Bangladesh is comparatively high. Incidence found to be as low as 1% and as high as 15%.

A study done in middle east in a private clinic about 12% of the study sample had abnormal (precursors of cervical cancer) results and the majority (88%) had normal and benign changes so the place of study also influence the result because in private clinics usually symptomatic patients are presented.[29]

A large study done in Teheran with an organized screening program including 13315 pap smear showed abnormal smear 1.18%.[30]

In our study we also tried to find out the relationship between gross look of cervix and result of pap smear. We had incidence of abnormal smear of less than 1% among healthy cervix and 1.2% among unhealthy cervix. Similar study was carried out by Pradhan B and found the malignancy as high as 15% among unhealthy looking cervix and it was confirmed by cervical biopsy.[31]

As we had 20 cases of different grades of abnormal epithelial abnormalities. For LSIL, we treated them with antibiotics and took smear after 3 months. Those who had same result on follow up smear were subjected for cervical biopsy. All five cases of smear with HSIL and 9 cases of LSIL had cervical biopsy (6 cases of LSIL were negative on repeat smear). Out of 5 cases of HSIL, 2 had biopsy proven HSIL, 2 had LSIL and 1 had chronic cervicitis. Out of 9 cases of LSIL, 3 had chronic cervicitis and 6 had LSIL. Total cases of abnormal finding by smear were 20.

Americal College of Obstetrician and Gynecolology (ACOG) recommended guideline for cervical cancer screening- 2012.[32]

A. when to start screening

Age 21 regardless of the age of sexual activity. Women aged <21 years should not be screened regardless of age at sex rega of sexual and other behavior-related risk factors

About annual screening

In women aged 30–65 years, annual cervical cancer screening should not be performed. Patients should be counseled that annual well-woman visits are recommended even if cervical cancer screening is not performed at each visit.

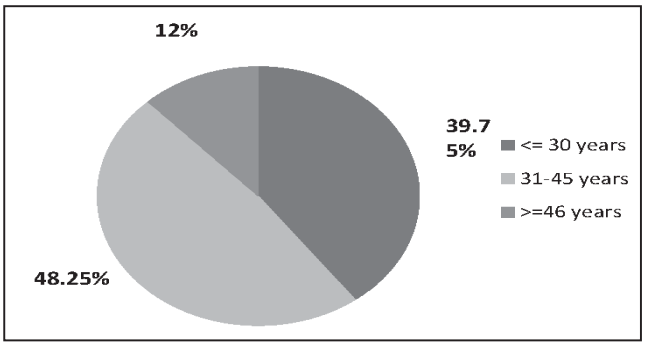

Fig. 1. Age distribution

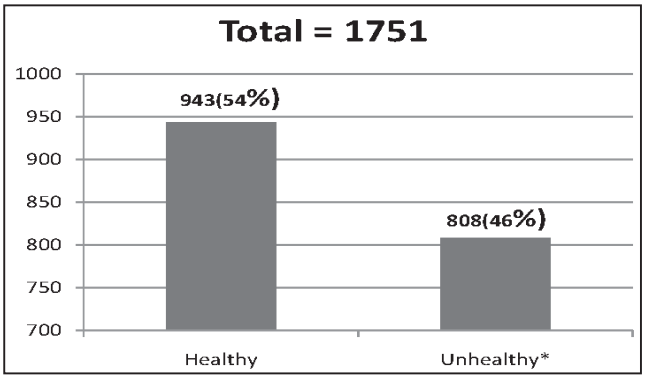

Fig. 2. Gross look of cervix
(*Unhealthy = Erosion, hypertrophied, congested, growth)

	Pap reports				
Gross Cx	Normal*	Percentage	Abnormal*	Percentage	Total
Healthy	935	99.1%	8	0.8%	943
Unhealthy	796	98.5%	12	1.4%	808
total	1731		20		1751

Normal smear* = Normal, Inflammatory and ASCUS; Abnormal smear*= LSIL,HSIL,CIS; None of them were carcinoma in situ

Reports of Smear

S.N	Reports	Number	Percentage
1.	Normal	571	32.60%
2.	Inflammatory	1152	65.79%
3.	ASCUS	8	0.45%
4.	LSIL	15	0.85%
5.	HSIL	5	0.28%
6.	CIS	0	0%
	TOTAL	1751	100

ASCUS is taken as normal since this is not a premalignant condition Therefore, it shows that majority of the smear were with inflammatory pattern accounting for 65.8% of the total smear and it was mainly prevalent in the age group 30-60 years. Out of 20 cases of abnormal smear 14 had biopsy and 10 had biopsy proven ab normal smear.

Frequency of screening

Every 3 years for conventional cytology and liquid base cytology

Every 5 years in case of conventional and HPV co-testing

HPV co-testing should not be performed in women aged < 30 years.

B. When to stop

Aged >65 years with adequate screening history(having hysterectomy done for some other reason beside precancerous and cancerous lesion)

Women who have received the HPV vaccine should be screened according to the same guidelines as women without vaccination.

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