

Pap's Test Result Proved by Colposcopy and Directed Biopsy in Bangabandhu Sheikh Mujib Medical University

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Abstract

Introduction: Cervical cancer is the second most common cancer in female with high morbidity and mortality. Worldwide, cervical cancer is the fourth most occurring malignancy and results in an estimated 530,000 new cases annually with 270,000 deaths. In many developed countries, health education, awareness programs and early detection and appropriate management achieve 80% reduction in mortality. Cervical cancer death is successfully prevented in developed countries by cervical cytology screening. **Methods:** This was a comparative cross sectional study conducted in Gynaecological Oncology Department of Bangabandhu Sheikh Mujib Medical University. Duration of the study was one year from July 2018 to June 2019. It was aimed to evaluate the performance status of Pap's smear as a screening test for cervical cancer. Sample size was Hundred and Pap's smear were collected at GOPD. Cytology of the sample were done by conventional method. All the patients underwent colposcopy and directed biopsy at the colposcopy clinic of Gynae Oncology. **Result:** The result shows maximum (44%) patients had first intercourse at 10-15 years of age. Maximum (72%) patients came from low socioeconomic condition. The specificity and positive predictive value of pap's test was found as 81% and 52.63% respectively. According to pap's report 19% patients were positive and according to colposcopy biopsy 59% patients were positive for cervical intraepithelial neoplasia. **Conclusion:** Cervical cancer screening for the early diagnosis of CIN, pap's smear is mandatory. VIA as a screenings test is not sufficient for the postmenopausal women.

Key words: Screening test, Cervical Cancer, Pap's smear, colposcopy directed biopsy.

Number of Tables: 04; Number of References: 12; Number of Correspondences: 04.

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Introduction:

Cervical cancer is the second most common cancer in female with significant cause of morbidity and mortality worldwide¹. Worldwide, cervical cancer is the fourth most frequently occurring malignancy in women, and results in an estimated 530,000 new cases annually with 270,000 deaths. Approximately 85% of the worldwide deaths from cervical cancer occur in underdeveloped or developing countries, and the death rate is 18 times higher in low-income and middle-income countries compared with wealthier countries^{2,3}. The highest incidence rates occur in Central and South America, the Caribbean, Sub-Saharan Africa, and Southern Asia⁴. In the United States in 2016, there were an estimated 12,990 cases and 4120 deaths from cervical cancer⁵. Among Latin-American women, cervical cancer is the leading cause of cancer deaths. Cervical cancer constitutes about 21-35% of the female cancer

in different areas of India and Bangladesh^{6,7}. Cervical cancer is also an indicator of health inequities as 86% of all deaths due to cervical cancer are in low income and developing countries⁸. It has been well documented that the disease develops from well-defined precursor lesion named CIN or cervical intraepithelial neoplasia, progression of which depends upon persistence of high risk group of HPV (Human Papilloma Virus) infection. Of the several known oncogenic HPV types, HPV types-16 and 18 are two most prevalent; worldwide, they are responsible for approximately 70% of invasive cervical cancers and approximately 50% of CIN grades 2 or 3⁹. In many developed countries, health education, awareness programs and early detection and appropriate management achieve 80% reduction in mortality⁸. Cervical cancer death is successfully prevented in developed countries by cervical cytology screening. However, in developing countries, screening programs have not had the same impact in women's health. Reasons for the lack of effectiveness of these screening programs in developing countries include low screening coverage and participation rates among women's, lack of quality control, poor ability of the health care system to offer proper follow-up and access to colposcopy, and inappropriate final diagnosis and treatment. While deficiencies associated with the quality control and follow-up aspects of cervical cancer screening programs must be confronted at an administrative and regulatory level, problems with rates of participation of women in cervical cancer prevention programs might be addressed by examining population, attitudes and trends. There is no doubt that when women face participation decisions, it is ideal for them to have a good understanding and perception of the risks of acquiring cervical cancer and the benefits of preventing it⁷. In many developed countries, health education, awareness programs and early detection and appropriate management achieve 80% reduction in mortality⁶. A colposcope is a low-power, stereoscopic, binocular field microscope with a powerful light source used for magnified visual examination of the uterine cervix to help in the diagnosis of cervical neoplasia. The most common indication of referral for colposcopy is positive screening tests (e.g positive cytology, and positive VIA. The key ingredients of colposcopic examination are the observation of features of the cervical epithelium after application of normal saline, 3-5% dilute acetic acid, and Lugol's iodine solution in successive steps. It is important to carefully document the findings of colposcopic examination, immediately after the procedure, in a colposcopic record. The practice of colposcopy is a cornerstone of cervical cancer prevention. In conjunction with screening and treatment of precancers, colposcopy has played a pivotal role in reducing the incidence and mortality from cervical cancer over the past 50 years^{9,10,11}. To confirm the test result of a screening test it is necessary to find out the sensitivity, specificity, false positive and negative result, positive predictive value and negative predictive value of the test. To find out these values of pap's test, a tissue from the cervix will be taken under colposcopic guide and sent for histopathological examination. After getting reports of cytology, colposcopic examination and biopsy report, all the values of pap's test will be found out by Statistical analysis. As

pap's test is an international screening test, we should improve these values of this test. From this study we will be able to find out the defaults of the test procedure. Further we will try to cover up these defaults.

Methods:

This cross-sectional and hospital based study was carried out at the colposcopy clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU) between July 2018 to June 2019. The women attending the GOPD of BSMMU having normal cervix was invited to participate in the study. The procedure was explained, and women who agree to participate were recruited after written informed consent. Pap's smear was collected, cytological study of the cervical samples obtained by Ayre's spatula was done by conventional cytology method. In all patients colposcopy was performed and biopsy was taken. Cytological, and histological investigations was conducted in the pathology department of BSMMU.

Sample size

The prevalence of cervical intraepithelial neoplasia in Bangladeshi women is not known, the minimum sample size can be determined by the following formula:

$$N = (Z^2 pq) / d^2$$

Where,

N = The desired sample size

Z = The standard normal deviate, usually set at 1.96 which corresponds to the 95% confidence level

P = The proportion in the target population estimated to have a particular characteristic. As there is no known estimate, then 50% can be used. $q = 1.0 - p$. d = Degree of accuracy desired, usually set at .05

$$N = ((1.96)^2 (.50)(.50)) / (.05)^2$$

= 384 women required.

Considering the time constraints and other limitations 105 cases were recruited

Selection Criteria:

The ultimate objective of the research was to select the women of reproductive age between 20-50 years. These women were selected by examining their cervix. Abnormal looking cervix was excluded. Only normal looking cervix was tested. First of all cervical scraping will be collected by Ayre's spatula from both endo and exocervix. Smear will be made, then the slide sent to the laboratory for cytological examination. Ultimately cervix will be examined by colposcope in 10-15 magnification and biopsy will be taken by Trishler's forcep. Biopsy specimen was sent to the pathology department of this university for histopathological examination. Results will be collected by specified persons of the project. All the data will be collected in a predesigned questionnaire form and the data will be statistically analyzed.

Sample collection:

A pap smear was collected from cervix using Ayre's spatula and cytobrush. that adequately sample both endocervix and ectocervix. Sampling of the transformation zone was performed first. The endocervical canal was then sampled by inserting the pointed end of the spatula rotating no more than 180 degrees to minimize bleeding. The samples were smeared immediately on to slide and immersed in Koplin's jar containing 95% ethyle alcohol for prompt fixation of the collected cells and to avoid air drying. The slide of the pap's smear was sent to the pathology department of the university

for preparation and interpretation.

All the cervixes were examined by colposcopy. During colposcopy biopsy specimen was collected by Trischler's punch biopsy forcep from all the cervixes as a back up of test result. Biopsy specimen was sent to the pathology department of BSMMU for histological examination.

Data collection Instruments

A pretested questionnaire was used as data collection instrument. After counseling and motivating the study population, data was collected from cases at colposcopy clinic by face to face interview by trained Research Assistant under supervision of principal investigator. The interview questionnaire was collected information about socio demographic and reproductive health characteristics. All the reports of pap's smear, colposcopy and histopathological examination was collected by trained Research Assistant and recorded in the data collection sheet.

Statistical analysis:

Completed interviews was reviewed, edited and processed for computer data entry. The data was entered and the data analysis was performed using Statistical Package for the Social Science (SPSS) program software version: 13.

Ethical Consideration:

Ethical clearance was taken from the ethical clearance committee of department of Gynaecological Oncology of BSMMU. Moreover an informed written consent was taken performing the procedures.

Result:

The Results are shown in tables

Table-I: Demographic characteristics of respondents (n=105)

Parameters	Range	Mean±SD	No.	(%)
Age (years)				
20-30	21.00-67.00	41.18±10.20	17	(16.2)
31-40			44	(41.9)
41-50			24	(22.9)
>50			20	(19.0)
Age (years) at 1st intercourse				
10-15	11.00-38.00	17.59±4.80	46	(43.8)
16-20			39	(37.1)
21-25			12	(11.4)
26-30			6	(5.7)
>30			2	(1.9)
Age (years) at marriage				
10-15	10.00-40.00	17.76±5.43	46	(43.5)
16-20			39	(37.1)
21-25			13	(12.4)
26-30			4	(3.8)
>30			3	(2.9)
Duration of sexual activity (years)				
10-15	2.00-54.00	22.96±10.91	10	(9.5)
16-20			19	(18.1)
21-25			20	(19.0)
26-30			17	(16.2)
>30			15	(14.3)
			24	(22.9)
Socioeconomic status				
Low			29	(27.6)
Middle			76	(72.4)
High			0	

Table-I shows the basic data of the study subjects. mean age of the patients were 41.18±10.20, range was 21-67 years and highest number of patients were in the age group 31-40 years. Mean age of first intercourse was 17.59±4.80, range was 11-38 years and maximum (43%) patients started their sexual activity at 10-15 years of age. Age at first intercourse

and age of marriage were more or less similar. Regarding duration of sexual activity 23% women had more than 30 years of sexual activity. 72.4% patients come from middle class family and 27.6% women come from lower socioeconomic class. None of the women came from higher socioeconomic class.

Table-II: Biopsy and diagnostic efficacy for cervical intraepithelial neoplasia (CIN) (n=105)

Efficacy (%)	Pap's smear	Colposcopy
Sensitivity	17.24	34.48
Specificity	80.85	76.60
Positive predictive value	52.63	64.52
Negative predictive value	44.19	48.65
Accuracy	45.71	53.33

Table-II shows the specificity, sensitivity, positive predictive value, negative predictive value and accuracy of pap's smear and colposcopy biopsy. All the parameters of pap's smear are lower than colposcopy biopsy except specificity which is higher for pap's smear.

Table-III: Biopsy and efficacy of pap's smear test for cervical intraepithelial neoplasia (CIN) (n=105)

	Pap's smear for CIN		Biopsy for CIN	
	No.	(%)	Positive No.	(%)
Positive	19	(18.1)	10	(17.2)
Negative	86	(81.9)	48	(82.8)
Total	105		58	(55.2)

Sensitivity	:	17.24%
Specificity	:	80.85%
Positive predictive value	:	52.63%
Negative predictive value	:	44.19%
Accuracy	:	45.71%

Table-IV: Biopsy and efficacy of colposcopy test for cervical intraepithelial neoplasia (CIN) (n=105)

	Colposcopy for CIN		Biopsy for CIN	
	No.	(%)	Positive No.	(%)
Positive	31	(29.5)	20	(34.5)
Negative	74	(70.5)	38	(65.5)
Total	105		58	(55.2)

Sensitivity	:	34.4%
Specificity	:	76.60%
Positive predictive value	:	64.52%
Negative predictive value	:	48.65%
Accuracy	:	53.33%

Table-IV shows details of these two test results.

Discussion:

Most of these women were referred from the GOPD of BSMMU. Women having complain of excessive vaginal discharge were mainly referred for pap's smear. Very few patients came from some private clinics. All women had pap's smear and colposcopy directed biopsy. Abnormal pap's smear reports were confirmed by colposcopy and directed biopsy. In this regard pap's report was found highly specific. This specificity of pap's report can be further improved by liquid based cytology. In liquid based cytology, sample is collected by specially designed cytobrush. The brush scrap both endocervix and exocervix by which chance of missing abnormal area is very low. Another advantage of LBC is that the sample is directly immersed in liquid media by which all the cells are preserved in the media. Third advantage of LBC is that the sample is centrifuged by which dead cells and debris are removed before smear formation. The smear become accurate, clean, only the fresh cells are remained in

the slide. So, specificity of the pap's test can be highly increased. Many components are needed to establish an effective cytology programme on a wide scale. Governmental/national support and recognition of the need for screening and treatment and the burden of disease per specific area are required to gather appropriate funding⁷. Culturally appropriate education of women and healthcare providers may help ensure compliance with screening recommendations that require more than one cytology exam to increase efficacy. Training personnel such as cytology technicians is necessary to provide follow up for cytology findings. All screening efforts, including cytology, can only be effective if diagnostic and treatment modalities are available and accessible. In low resource settings, particularly developing countries, evidence indicates investments in cytology have not yielded adequate results. For this reason, other screening modalities covered in this guidance should be explored to improve and expand current efforts. In the present study 31-40 years age group with median age 41.18±10.20 was the most common group resembles the age group of study of Gandavaram J. Women with early sexual exposure in early life and more children are associated with more chance of abnormal findings in screening for cervical premalignant lesions⁸. In this study the sensitivity of pap's smear test was found 17.24%, specificity-80.85%, positive predictive value-52.63%, negative predictive value-44.19% and accuracy of pap's test was 45.71%. Whereas in colposcopy sensitivity 34.48%, specificity 76.60%, positive predictive value 64.52%, negative predictive value 48.65% and accuracy is 53.33%. All the parameters pap's smear are lower than colposcopy biopsy except specificity which is higher for pap's smear. In another study of Khatun S showed higher sensitivity in colposcopy than pap's test which resembles with the present study¹². In this study pap's smear positive 18.1% (n=19) colposcopically 29.5% positive (n=31). In pap's positive cases biopsy positive for CIN is 17.2% (n=10) whereas colposcopically biopsy positive for CIN in colposcopy positive were 34.5% (n=20).

Conclusion:

From this study we came to the conclusion that for the screening of cervical cancer for the early diagnosis of CIN, pap's smear is mandatory. Because VIA as a screenings test which is not sufficient for the postmenopausal women. Previous idea about pap's smear that it gives more false negative results, can be overcome by training of the doctors, by using liquid based cytology and by taking endocervical sample.

Recommendation:

Our recommendation about pap's smear is that this gold standard screening test should be used in all levels of gynaecological patient care. For this purpose, junior doctors should be trained up by appropriate program.

Conflict of Interest: None.

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