Original Article

Evaluation of Liquid Based Cytology (LBC) and Conventional Pap's Smear Test as Methods of Cervical Cancer Screening

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Abstract:

Background: Cervical cancer screening can actually prevent most cervical cancers and also facilitates early detection which allows fruitful treatment. ***Objective:*** To evaluate and compare the efficacy of Liquid-based cytology (LBC) with conventional Pap smear test. ***Methods:*** This cross-sectional study was conducted between March 2015 and June 2017. A total of 72 women participated in this study attending the Out-Patient Department (OPD) of Gynaecology (Colposcopy Clinic) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, for VIA test. The smears prepared by the conventional Pap smear method and Liquid-based cytology method were observed by two independent observers in Department of Pathology of the same institution. ***Results:*** The mean age of the patients was 40.22±12.29 years. Considering histopathology as gold standard, in conventional Pap smear preparation our data suggested its sensitivity 87.5%, specificity 92.2%, accuracy 91.7%, positive predictive value 58.3% and negative predictive value 98.3%. In contrast, in Liquid-based cytology, we found its sensitivity 75.0%, specificity 90.6%, accuracy 88.9%, positive predictive value 50.0% and negative predictive value 96.7%. ***Conclusion:*** LBC has practical advantages over conventional preparation by producing monolayer of cells, smaller area to screen, reproducibility and availability of doing adjunct molecular techniques from residual sample. However, conventional preparation shows better sensitivity and positive predictive value and almost similar specificity, negative predictive value and accuracy with LBC.

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Introduction:

Early detection of cervical cellular changes and cervical intraepithelial neoplasia (CIN) followed by appropriate treatment will reduce the risk of developing cancer[1]. Screening tests offer the best chance to have cervical cancer found early when treatment can be most successful. Screening can also actually prevent most cervical cancers by finding abnormal cervical cell changes (pre-cancers) so that they can be treated before they have a chance to turn into a cervical cancer[1,2]. The implementation of population-based screening for cervical cancer with Pap smear in the early sixties was set to detect and treat precancerous lesions, hopefully preventing a subsequent invasive cervical cancer. Thus, Pap smear has been utilized for cervical cancer screening for more than 50 years[2,3]. Despite being credited with a 70%

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reduction in mortality for cervical cancer, the false negative rate is still a cause for concern[4,5]. It is widely acknowledged that two third of the overall false negative rate can be attributed to sampling errors. Liquid based cytology has been developed to address the sampling problems of conventional Pap smear[4]. In some settings, liquid-based cytology (LBC) has replaced the conventional Papanicolaou (Pap) test, offering practical advantages[4,5]. The application of cells to the glass slide is standardized; cells are distributed evenly over the surface; mucus, blood, and inflammatory cells are reduced in the preparation; and fixation is effective and even[4,6]. However, in our country, there is no previous record of comparison between these two methods. Hence, the present work was done to evaluate the liquid based cytology and to compare its sensitivity, specificity and accuracy with the conventional Pap smear.

Methods:

This cross-sectional study was conducted between March 2015 and June 2017. The study population included women attending the Out-Patient Department (OPD) of Gynaecology (Colposcopy Clinic) of Bangabandhu Sheikh Mujib Medical University (BSMMU) for VIA test. Exclusion criteria included who do not give consent, pregnant women, patients with massive vaginal bleeding and patients of treated cervical carcinoma. Finally, a total 72 women were included in this study. The smears prepared by the conventional Pap smear method and Liquid-based cytology method were observed by two independent observers in Department of Pathology of the same institution. Endocervical broom brush (supplied by Becton Dickinson) was used to obtain sample. Brush was rotated against the ectocervix for a 360^0 rotation to include the transformation zone. Material on the brush was smeared onto a glass slide for conventional smear preparation and fixed in alcohol. The brush along with remaining material was detached and rinsed into a bottle containing liquid fixative containing 24% ethanol.

Conventional Pap smear: Cervical smear cells collected from the transformation zone of cervix was smeared upon a slide and fixed in 95% ethyl alcohol for at least half an hour. Then it was stained by conventional Pap's staining and examined under the microscope.

Liquid-based cytology method: Liquid based cytology was done by Beckton Dickinson Sure-path technique. Here, the cells were prepared at a monolayer by separating on concentration gradient with the help of sure path preparation made which produces a 13 mm^2 area of representative sample on the slide. It was then manually stained by stains supplied by Beckton Dickinson.

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS) version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Chi-Square test was used to analyze the categorical variables, shown with cross tabulation. Sensitivity, specificity, positive predictive value and negative predictive value for liquid-based cytology and conventional Pap smears were calculated. P value of <0.05 was taken as significant.

Results:

The mean age was found 40.22±12.29 years with range from 18 to 72 years. Most of the participants were in their reproductive age, while 23 (31.9%) were post-menopausal (Table 1). it was observed that smear unsatisfactory for evaluation was found in four cases by conventional preparation, all of them were chronic cervicitis. NILM was found in 56 cases as per conventional smear, among them one case was CIN-I and 55 cases were chronic cervicitis diagnosed by histopathology examination. ASCUS were found in nine cases among them four cases were CIN-I, five cases were chronic cervicitis. LSIL was found in one case and it was CIN-I. HSIL was found in two cases among them one case was CIN-II and one case was squamous cell carcinoma. The concordance between conventional preparation with histopathology was 87.5% (Table 2). In the study, it was observed that in LBC, ASCUS were found in four cases among them one case was CIN-I and three cases were chronic cervicitis. NILM were found in 60 cases among them two cases were CIN-I and 58 cases were chronic cervicitis. LSIL were found in two cases and both of those were CIN- I. ASC-H were found in five cases among them one case was CIN-I, one case was CIN-II and three cases were chronic cervicitis. Squamous cell carcinoma was found in one case which was proved histologically. The concordance between liquid based cytology with histopathology was 75.0% (Table 3). Considering

histopathology as gold standard, in conventional Pap smear preparation our data suggested its sensitivity 87.5%, specificity 92.2%, accuracy 91.7%, positive predictive value 58.3% and negative predictive value 98.3%. In contrast, in Liquid-based cytology, we found its sensitivity 75.0%, specificity 90.6%, accuracy 88.9%, positive predictive value 50.0% and negative predictive value 96.7% (Table 4).

Table 1. Distribution of the study respondents by age (N=72)

Age (in year)	Frequency	Percentage (%)
≤30	18	25.0
31-40	26	36.1
41-50	16	22.2
51-60	6	8.3
>60	6	8.3
Mean ±SD	40.22±12.29	
Range	18-72	

Table 2: Concordance between conventional preparation of cervical smear with histopathology (n=72)

Conventional preparation	N	Histopathology			
		CIN-I	CIN-II	Chronic cervicitis	SQ.C.C
Unsatisfactory	**4**	0	0	4	0
NILM	**56**	1	0	55	0
ASCUS	**9**	4	0	5	0
LSIL	**1**	1	0	0	0
HSIL	**2**	0	1	0	1
Total	**72**	**6**	**1**	**64**	**1**

NILM- Negative for Intraepithelial lesion or malignancy, ASCUS- Atypical Squamous Cells of Undetermined Significance , LSIL- Low grade Squamous Intraepithelial Lesions, HSIL- High grade Squamous Intraepithelial Lesions

Table 3: Concordance between liquid-based cytology of cervical smear with histopathology (n=72)

Liquid based cytology	n	Histopathology			
		CIN-I	CIN-II	Chronic cervicitis	SQ.C.C
NILM	**60**	2	0	58	0
ASCUS	**4**	1	0	3	0
LSIL	**2**	2	0	0	0
ASC-H	**5**	1	1	3	0
SQ.C.C	**1**	0	0	0	1
Total	**72**	**6**	**1**	**64**	**1**

NILM- Negative for Intraepithelial lesion or malignancy; ASCUS- Atypical Squamous Cells of Undetermined Significance; LSIL- Low grade Squamous Intraepithelial Lesions; ASC-H- Atypical Squamous Cells-cannot exclude HSIL; SQ.C.C -Squamous cell carcinoma.

Table 4: Sensitivity, specificity, accuracy, positive and negative predictive values of the conventional preparation and liquid based cytology for the prediction of atypical lesion in cervical smear

Validity test	Conventional preparation	Liquid based cytology
Sensitivity	87.5	75.0
Specificity	92.2	90.6
Accuracy	91.7	88.9
Positive predictive value	58.3	50.0
Negative predictive value	98.3	96.7

Discussion:

Karimi-Zarchi et al.[3] showed out of 150 patients the conventional Pap smear method had a sensitivity 51%, specificity 66.6%, positive predictive value 96%, negative predictive value was 88% and accuracy was 92%, about the liquid base Pap smear method, sensitivity was 55.3%, specificity was 77.7%, positive predictive value was 97.5%, negative predictive value was 10% and accuracy was 56.6%. Nandini et al.[5] showed out of 100 patients, the rate of concordance with histology was 77% for conventional Pap and 86% for LBC. The rate of increased detection of LSIL through LBC was 150%. In addition, to compare the validity of the two methods, they estimated sensitivity and specificity of the two

methods considering histopathology as the gold standard. Sherwani et al.[7] found that sensitivity and specificity of Pap spin was 97.6% and 50.0% respectively and of conventional Pap smear 53.7% and 50% respectively. Singh et al.[8] compared the performance of LBC and conventional cytology in an Indian setting. The detection rate of epithelial abnormalities and infections in both preparations was similar. Unsatisfactory rate of Pap smear was 4.3% and 1.7% for LBC, which was statistically significant. Another local study done by Nurunnabi & Sultana[9] reported that sensitivity and specificity of Pap's smear were only 55.55% and 98.58% respectively. Zhu et al.[10] showed the sensitivity for detecting a CIN-II+ lesion with conventional Pap smear was 47%, compared with 66% for LBC testing. When compared with other studies comparing between LBC and conventional preparation, our study showed almost similar specificity, accuracy and negative predictive values among these two methods and higher sensitivity and positive predictive value for conventional method which is consistent with most of the studies. In contrast, Strander et al.[6] reported that in cervical screening program of western Sweden, liquid cytology produced a significantly higher yield of histologic high-grade lesions compared with conventional Pap smears.

Limitations of the study:

The study population was selected from one tertiary care hospital in Dhaka city; hence, the results of the study may not reflect the exact picture of the country. Small sample size was also a limitation of the present study. Therefore, in future further studies may be undertaken with larger sample size and multi-centre approach throughout the country.

Conclusion:

To summarise, LBC has practical advantages over conventional preparation by producing monolayer of cells, smaller area to screen, reproducibility and availability of doing adjunct molecular techniques from residual sample. However, conventional preparation shows better sensitivity and positive predictive value and almost similar specificity, negative predictive value and accuracy with LBC.

Conflict of interest: The authors declare no conflict of interest.

Ethical approval issue: The study was approved by the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

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Authors' contribution: Conception and design of the study: MAC, ARB; Data collection and compilation: MAC, ARB, AZ, MMH, DMAR; Data analysis: MAC; Critical writing, revision and finalizing the manuscript: MAC, ARB, AZ, MMH, DMAR.

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