



The Comparative Evaluation of Liquid Based Cytology (LBC) and Conventional Pap Smear As a Screening Method of Cervical Cancer at Tertiary Care Center, Kota Rajasthan, India

Authors

Badri Lal Patidar¹, Suman Mendiratta², Neelam Meena³, Shivraj Meena⁴

¹Assistant Professor, Department of Obstetrics & Gynecology, Govt Medical College Kota, Rajasthan, India

²Professor, department of obstetrics & Gynecology, SMS Medical College Jaipur, Rajasthan, India

³Senior Resident, Department of Obstetrics & Gynecology, Govt Medical College Kota, Rajasthan, India

⁴Assistant Professor, Department of medicine, Govt Medical College Kota, Rajasthan, India

Corresponding Author

Dr Badri Lal Patidar

Assistant Professor Department of Obstetrics & Gynecology, Govt Medical College Kota, Rajasthan, India

Email: patidar.badri@gmail.com, Mobile 9414570937

Address – Type III/10, Medical College Campus, Govt Medical College Kota Rajasthan Pin Code 324005

Abstract

Objective: The comparative evaluation of liquid based cytology (LBC) and conventional Pap smear as a screening method of cervical cancer.

Method: This was a hospital based prospective study, based on 58 women presenting with gynecological complaints. Pap smears were taken from all these patients with Ayre's spatula and endocervical cytobrush and slides prepared. The residual material on both the spatula and cytobrush were rinsed in Pap spin collection fluid and centrifuged. Smears were prepared from the cell button, fixed and stained by Papanicolaou stain. Colposcopic guided cervical biopsy was taken from only dysplastic or suspected carcinomatous cases.

Result: Majority of patients belonged to fourth decade of life. Most common presenting complaint was persistent vaginal discharge or leucorrhoea present in 41(70%) cases. Low grade squamous intraepithelial lesions were found in 9(16%) cases on LBC as compared to 7(12%) cases on pap's smear whereas 4(7%) cases had HSIL on LBC as compared to 2(3%) cases on conventional pap's smear and 2 cases each had squamous cell carcinoma on LBC and pap smear. Sensitivity of Pap spin and conventional Pap smear was 87.5% and 62.5% respectively and specificity was 97.6% in each.

Conclusion: Liquid based cytology increases detection rate of low squamous Intraepithelial lesions (LSIL) and high squamous intraepithelial lesions (HSIL) than conventional pap smear and comparable to conventional pap smear in detecting squamous cell carcinoma. Therefore, the screening performance of liquid based cytology is superior to conventional cytology and this approach may be used alternative screening methods of cervical cancer.

Keywords: LBC, Pap smear, HSIL SCC.

Introduction

Worldwide, cervical cancer is the second most common cancer among women with an estimated 493,000 new cases occurring annually and 274,000 deaths occurring each year.¹ Cervico-vaginal cytology is a technique used successfully in early detection of pre and early cancers of the cervix. George Papanicolaou introduced cervical cytology into clinical practice in 1940². In 1945; the Papanicolaou smear received the endorsement of the American cancer society as an effective method for the prevention of cervical cancer. The standard technique for Pap smear collection is to sample the portio vaginalis of the cervix and the endocervical canal using a cervical spatula and endocervical brush. The collected sample is smeared on a slide and then fixed immediately with cytofixative. Most clinicians are concerned with reducing sampling errors by focusing on the technique of smear acquisition and eliminating drying artefacts' through rapid fixation.

There are various problems associated with conventional cytology incorrect and inadequate sampling in 5-10% of cases³ only up to 20% of harvested cells are transferred on the slide leading to a reduction in the sensitivity of the test³ Mean sensitivity of only 55-60%⁴. Reported false negative rates varying from 25 to 50%⁵ and false positive rates varying from 15 to 20%⁶. Park et al² established that the sensitivity of the conventional Pap smear for the detection of cervical cancer precursors was less than 50%.

Recently liquid based cytological technologies have been developed and have gained popularity because in preliminary studies the use of such techniques was associated with a reduction in the incidence of inadequate cervical smear. The present study was undertaken to evaluate a liquid based cytology technique (Pap spin) and to compare the sensitivity of Pap spin with conventional Pap smear.

Method

The Regional Committee approved the study protocol for Medical Research Ethics and all

participants gave informed written consent. This was a prospective study conducted from January 2016 to December 2016 in Department of Obstetrics & Gynecology Govt Medical College, Kota on 58 patients with gynecological complaints attending the inpatient and outpatient department. Patients were randomly selected based on complains like of abnormal vaginal bleeding, persistent vaginal discharge, pain in lower abdomen, post coital bleeding and any abnormal finding on per speculum examination.

After detailed history and written informed consent, conventional Pap smear taken by Ayre's spatula and endocervical cytobrush, slide was prepared and residual material on both spatula and cytobrush was rinsed in 10-15 ml of Pap spin collection, a buffered methanol preservative solution in vial. Pap smear slides and Pap spin collection fluid along with collected material was sent to laboratory for histopathology. In laboratory the Pap spin collection fluid along with collected material was centrifuged at 1500 rpm for 10 min then supernatant was discarded and direct smear was prepared from cell button and fixed in cytofixative with equal part of 95% ethyl alcohol and ether for at least 20 minutes and then in both type of slides staining was done by standard Papanicolaou method and reporting was done according to revised Bethesda system. After reporting patients with suspected malignant or dysplastic changes were subjected to colposcopic guided cervical biopsy. The biopsy specimen was fixed in 10% formalin labeled and sent to pathology department for histopathological evaluation. Statistical analysis was performed with the statistical package for the social science system version SPSS 17. Variables are presented as absolute numbers and percentage. Nominal categorical data between the groups were compared using Chi-squared test as appropriate. $P < 0.05$ was considered statistically significant.

Result

This prospective study was carried out on 58 patients attending the inpatient and outpatient

department of Obstetrics and Gynecology, Govt Medical College & Hospital, Kota.

Maximum number of patients i.e. 54% belonged to age group 31-40 yrs and minimum number i.e. 3% in age group of >60 yrs. The mean age of case study was 41 yrs. Majority of cases 38 (66%) belonged to rural area and 37 (64%) were of lower socioeconomic class.

Most common presenting complaint was persistent vaginal discharge or leucorrhoea in 41(70%) cases, followed by pain lower abdomen in 33(57%) cases, excessive or irregular bleeding in 22(38%) cases, postcoital bleeding in 9(16%) and foul smelling discharge in only 1(2%) case.

Out of total 58 cases, 9 (16%) cases has LSIL on LBC as compared to 7 (12%) cases on pap's smear. Four (7%) cases had HSIL on LBC as compared to two (3%) cases of HSIL on conventional pap's smear. Two cases had squamous cell carcinoma on each had squamous cell carcinoma on Pap smear Liquid Based Cytology. (table 1)

Eight cases were positive on both LBC and conventional Pap smear but seven cases which had positive cytology on liquied based cytology were negative on conventional Pap smear. Out of total 11 cases, that were positive on conventional Pap smear ,eight cases detected by liquid based cytology but three cases were missed on LBC.(table 2)

Out of total 16 cases, which were positive on cervical biopsy, 10 cases found positive on conventional pap's smear and 6 cases, found negative on pap's smear. Therefore, sensitivity of conventional pap's smear was 62.5%. One case, which was negative on pap's smear (Positive on LBC), was also negative on biopsy. Therefore, specificity of test was 97.6%.(table 4)

Out of total 16 cases positive on Biopsy, 14 cases were positive on LBC, so sensitivity of liquied based cytology was 87.50%. One case which was negative on LBC (Positive on Pap smear) also negative on biopsy, so test specificity, was 97.6%. (table 5)

On colposcopic, out of total 18 cases, 6 cases had colposcopic grade 1, 10 cases had colposcopic grade 2 and two cases had colposcopic grade 3.

Majority of dysplastic cases or carcinomatous cases (87%) had STD or history of STD as many of epidemiologic studies have shown a pattern of cervical cancer that is typical for sexually transmitted disease.

Total 20 cases, which had difference between age of menarche and first contact < 6yrs. Eight cases were negative for intraepithelial lesion, 6 cases had CIN1, 4 cases had CIN3 and 2 cases had SCC. Total 38 cases that had this difference >6 yrs, 34 cases were negative for intraepithelial lesion, three cases had CIN1 and one case had CIN3.(table 3)

Table 1 Case distribution according to Liquid Based Cytology and Pap's smear Grading in Bethesda system

	No. of Patients	Percentage (%)	No. of Patients	Percentage (%)
Normal	43	74.14	47	81.03
LSIL	9	15.52	7	12.07
HSIL	4	6.9	2	3.45
Carcinoma	2	3.45	2	3.45
Total	58	100	58	100

Table 2: Distribution of cases according to Pap's smear & Liquid base Cytological findings

Pap smear findings	Liquid based cytological findings		total
	positive	negative	
Positive	8	3	11
Negative	7	40	47
Total	15	43	58

$$\chi^2=12.679$$

$$d.f.=1$$

$$P< .001$$

Table 3: Association between age difference in Menarche and Ist contact with Histopathological Changes

Histopathological Changes	Difference between age of menarche and age of I st contact		Total
	≤6 years	>6 years	
Normal	8	34	42
CIN-I	6	3	09
CIN-III	4	1	05
Sq. cell carcinoma	2	0	02
Total	20	38	58

Table 4: Comparative study of PAP's smears findings with Histopathology

Pap Smear Report	Histopathological Report		Total
	Test + ve	Test - ve	
Test + ve	10	1	11
Test - ve	6	41	47
TOTAL	16	42	58

$\chi^2 = 23.476\%$ P<0.01 sensitivity= 62.5% specificity= 97.61%

Table 5: Comparative study of LBS findings with Histopathology

Liquid Based Cytology Report	Histopathological Report		Total
	Test + ve	Test - ve	
Test + ve	14	1	15
Test - ve	2	41	43
TOTAL	16	42	58

$\chi^2 = 39.455$ P<0.01 sensitivity= 87.50% specificity=97.61

Discussion

Age distribution of cases in the study with gynecological complaints between 25 yrs to 70 yrs of age. Maximum number of patients i.e. 54% were belong to age group 31-40 yrs of age. Although invasive cancer of cervix reported at all ages, even at birth, it now has two peaks one at above 35 yrs and another at 50-55 years following which there is reduced incidences.

In our study maximum cases with cytological abnormality, belonged to class III or below. This finding was similar to that noted by Christopher son and Parker (1960)⁷ who noted a high incidence of disease in women of low socio-economic class with younger age of marriage and child bearing.

In our study most common presenting complained was persistent vaginal discharge or leucorrhoea in 41(70%) cases, which was almost similar to Sherwani RK et al (2006)⁸ in this study most common presenting complained was discharge per vagina (43%).

In both test Pap smear maximum abnormal cases found in age group 31-40 yrs as similar to Singh Uma et al (2006)⁹ in this distribution of cases of CIN in different age group showed that 4.35%

were in <25 years of age group, 52.4% in 26 to 35 years age group, 26.09% in 36 to 45 years age group, and 17.39% in >45 years of age group.

The comparative evaluation shows 9 (16%) cases had LSIL on LBC as compared to 7 (12%) cases on pap's smear so that LBC was superior to conventional pap's smear to detect LSIL. 4(7%) cases has HSIL on LBC as compare to 2(3%) cases had HSIL on conventional pap's smear so that LBC was superior to detect HSIL lesion 2 cases had sq. cell carcinoma on LBC same had sq. cell carcinoma on pap smear so that LBC was comparable to pap' smear in detecting squamous cell carcinoma. LBC had 4% more positivity to detecting LSIL than pap's smear. LBC had 3.5% more positivity to detecting HSIL than pap's smear. LBC had comparable positivity to detecting sq. cal carcinoma to conventional pap's smear. As J Monsonego et al (2000)¹⁰ in this study on initial screening, 29 % more ASCUS cases and 39% more low-grade squamous intraepithelial lesions (LSIL) and more severe lesions (LSIL+) were detected on the Thin Prep slides than on the conventional smears (P=0.001), including 50% more LSIL and 18% more high-grade SIL (HSIL). As similar to M Tunc Canda et al(2009)¹¹ in this

study liquid based cytology showed significant decrease in the rate of unsatisfactory smears ($p < 0.01$) and the detection rate for atypical squamous cells was significantly higher ($p < 0.01$). The rate of low-grade squamous intraepithelial lesion was also higher. The number of high grade squamous intraepithelial lesions detected was increased with LP, and the histological correlation of LSIL lesions showed a higher positive predictive value.

Sensitivity of conventional pap's smear was 62.5% With P value ($p < 0.01$) that was significant. specificity of conventional pap smear was 97.6% sensitivity of liquid based cytology was 87.50% and specificity was 97.6% with P ($< 0.01\%$) and was Significant.

So that compare two proportion for sensitivity and specificity the p value is significant for sensitivity. Sheet et al.(1995)¹² measure smear sensitivity & specificity was 67.3% and 76.9% and LBC sensitivity & specificity was 73.6% and 76.2% as comparable to our study. Hutchinson et al. (1999)¹³ in this study the sensitivity of conventional pap smear was 68.7% whereas sensitivity of, LBC was 87.9% where LSIL or above based on a final diagnosis that was made by a combination of cytology, histology and cervicography.

Majority of dysplastic cases 10 out of 14 (71%) were multipara ($>P3$) and 2 cases of SCC one had parity = P3 and other was multipara a finding concordant to the studies of Shankarnarayana et al¹⁴ also commented that seven or more full term pregnancies had a fourfold increase in the risk of developing squamous cell carcinoma of the cervix.

In the study, 12 (75%) dysplastic or carcinomatous cases a difference of ≤ 6 years between age of menarche and age of first contact. None of previous studies had shown this correlation. P value for this correlation $P = 0.001$ which was significant

Out of total dysplastic cases 9 out of 14 (64%) and 2 carcinomatous cases (100%) had first conception before the 20 years of ages. Our study revealed majority of dysplastic cases 9 (64%) and

carcinomatous cases (2(100%)) had 1st contact at or before 18 years of ages as reported by Rotkin.¹⁵ ,postulated that carcinoma of cervix is a disease transmitted from male to female during intercourse, with a higher probability of occurrence with early age at first coitus. Majority of dysplastic, 10(71%) or carcinomatous cases 2(100%) had marriage below the 18 years of age.

Conclusion

From the above study, we can conclude that liquid based cytology increases detection rate of low grade squamous intraepithelial lesions (LSIL) and high grade squamous intraepithelial lesions (HSIL) than conventional pap smear and comparable to conventional pap smear in detecting squamous cell carcinoma. Therefore the screening performance of LBC is superior to conventional cytology and this approach may be used as alternative screening method of cervical cancer.

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