

Comparison of Liquid-based Cytology and Conventional Papnicolaou Smear as a Screening Tool in High-risk Females

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ABSTRACT

Introduction: Cervical cancer is the second most common cancer in women in India. Certain high-risk behavior is associated with an increased incidence of cervical cancers. Detection of its premalignant lesions is of utmost importance, which can be easily done by screening methods such as conventional Pap (CP) and liquid-based cytology (LBC).

Aim: The aim of the present study was to ascertain the effectiveness of CP and LBC as screening methods in high-risk group females and to determine if any one method is superior to the other.

Materials and methods: This study was conducted over a period of 6 months at SN Medical College, Agra. All high-risk group females were included in the study and paired samples for CP and LBC were collected from such patients. A total of 40 such cases were encountered during our study period. Patients having abnormal vaginal bleeding with known uterine or hormonal cause and known case of invasive carcinoma cervix were excluded from the study.

Results: A maximum number of cases were in the reproductive age group, most common age of presentation being 31–40 years (35%) followed by 20–30 years (32.5%). A majority of patients were presented with a history of early sexual activity (<18 years) (52.5%), followed by multiparity (25%). Overall CP had 100% sensitivity while LBC had a sensitivity of 91.6%. However, LBC detected one additional case of ASCUS and two additional cases of HSIL over CP. So LBC detected more cases but with a slightly decreased sensitivity over CP.

Conclusion: Both the screening methods are very effective and sensitive in the detection of premalignant lesions with slight discordance of grade on histology. Thus, we conclude that cervical cytology is very effective in the detection of premalignant lesions with the sensitivity of almost 100%. In developing countries such as India, where finances pose a major problem, conventional method is as good as LBC.

Keywords: Conventional Papnicolaou smear, High-risk females, Liquid-based cytology.

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INTRODUCTION

Cervical cancer is the second most common cancer in women in India.¹ So detection of its premalignant lesions is of utmost importance, which can be easily done by screening methods. The mainstay of cervical cancer screening is Papnicolaou (Pap) smear. Morbidity and mortality from cervical cancers have been shown to decrease substantially by the proper implementation of screening methods.²

Sexually transmitted human papillomavirus (HPV) infection is the most important risk factor for morphologic continuum of squamous alterations.³ Other factors include the age group of 35–45 years, coitus before 18, first delivery before 20, and multiple sexual partners.

Liquid-based cytology (LBC) has been approved by the US Food and Drug Administration to enhance the yield of a conventional Pap (CP) smear for cervical samples processing.⁴ The advantages of LBC are decreased number of unsatisfactory smears, clean background, an even distribution of cellular material, HPV testing by using residual cellular material, and decreased screening time.⁵

The aim of this study was to study the effectiveness of CP and LBC as a screening method in high-risk group females and to determine if any one method is superior to the other.

MATERIALS AND METHODS

This study was conducted over a period of 6 months at SN Medical College, Agra. All high-risk group females (postmenopausal bleeding, postcoital bleeding, early sexual activity before 18,

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multiple sexual partners, multiparity, and delivery before 20 years) presenting in the gynecology OPD were selected for paired samples of a conventional pap and liquid-based cytology. Patients having a satisfactory smear on both CP and LBC were included in the study. A total of 40 such cases were encountered during our study period. Patients having abnormal vaginal bleeding with a known uterine or hormonal cause and a known case of invasive carcinoma of cervix were excluded from the study. A detailed history with relevant clinical examination was undertaken. All patients underwent a pap testing. Ayer's spatula was introduced into the external cervical os and scraped to collect cells from ectocervix and endocervix. A smear on a glass slide was made and fixed. Then cytobrush was introduced and cells were collected. Cytobrush was then dropped in a vial of preservative fluid. Cervical smears prepared were stained

with the papanicolaou stain and were studied for adequacy and any cytological abnormality. Histology of premalignant lesions was sought, which correlated with cytological findings. Biopsy of 13 such cases was retrieved. Sensitivity of both the screening methods was calculated. In calculation of sensitivity, any positive finding on histology (whether LSIL, HSIL or carcinoma) was considered true positive, even if the grade of premalignant lesion on histology was discordant with that reported on cytology.

RESULTS

In this study, 40 patients were studied with an aim to compare the yield of liquid-based cytology with a CP in high-risk group patients. The age of the patients ranged from 20- to 70 years. A maximum number of cases were in the reproductive age group, with the most common age of presentation being 31–40 years (35%) followed by 20–30 years (32.5%).

A majority of patients were presented with a history of early sexual activity (<18 years) (52.5%), followed by multiparity (25%). The history of multiple sexual partners was difficult to elicit, which might be a cause of a comparatively low number of cases (2.5%) (Table 1).

An estimated 24 of 40 cases were categorized as NILM by both methods, and 29 were detected by LBC and 32 by CP. Similarly, one case was categorized as ASCUS by both, whereas LBC detected one additional case of the same. Four cases were categorized as LSIL by both the methods, whereas one additional case was detected by each method. Two cases of HSIL were detected by both, with two additional detections by LBC. Overall, 31 of 40 cases were of the same category by both the methods (Table 2).

Biopsy of all abnormal cases on cytology along with one normal case on cytology was undertaken. Histopathological findings were compared with cytological findings. On LBC, two cases reported as ASCUS turned out to be LSIL on histology, giving a sensitivity of 100%. Among five cases of LSIL on LBC, one case was reported as chronic cervicitis and four were reported as LSIL on histology, giving a sensitivity of 80% (Fig. 1A). On histological evaluation of four cases of HSIL, two were reported as LSIL and one each as

HSIL and squamous cell carcinoma, giving a sensitivity of 100% (Table 3 and Fig. 2A).

On CP, one case reported as ASCUS turned out to be LSIL on histology, giving a sensitivity of 100%. Among five cases reported as LSIL on CP revealed a 100% sensitivity as all were LSIL on histology (Fig. 1B) On histological evaluation of two cases of HSIL, one was reported as LSIL and one as squamous cell carcinoma, giving a sensitivity of 100% (Table 4 and Fig. 2B).

In our study, the sensitivity for a conventional PAP was higher for LSIL cases in comparison to LBC method; however, for all other categories, the sensitivity of both CP and LBC was equal as a screening tool for detecting positive abnormal cases.

The overall CP had 100% sensitivity while LBC had a sensitivity of 91.6%. However, LBC detected one additional case of ASCUS and two additional cases of HSIL over CP. So LBC detected more abnormal cases but with a slightly decreased sensitivity over CP.

DISCUSSION

A Pap smear is a useful and an important method for cervical cancer screening. Worldwide, there have been efforts to prevent cervical cancer by screening women using PAP smears and thereby detecting and treating the precancerous lesions.⁶ Cervical cancer incidence can be reduced by as much as 90% in a population undergoing regular screening and having high quality and coverage.⁷ However, in developing countries, due to lack of education and awareness, many women have never had a Pap smear. Thereby, proper implementation of screening program is the need of the hour.

According to American Cancer Society, women between 30 and 65 years of age should have a PAP test and HPV test every 5 years. Women at a high risk for cervical cancer should be screened more often. A Pap smear is a cytological test designed to detect abnormal cervical cells. The low sensitivity of a single Pap test makes it necessary to screen women relatively frequently, every 3–5 years.⁶

LBC is an alternative technique for screening and detection of precancerous lesions. In this method, the cells are washed into a vial of liquid and filtered, and the sample is prepared as a thin layer on a glass slide. These slides are either screened by a skilled person or are subjected to automated imaging. It is being widely used in many developed nations. Although these approaches appear promising, they are expensive and rely heavily on technology.⁶

LBC is considered superior to CP, even though its sensitivity and specificity is almost similar to CP as observed by many studies. This could be due to the fact that it produces consistently reduced rates of unsatisfactory smears, has improved sample processing, and better clarity on microscopy with an additional advantage of being able to perform HPV testing on the residual sample.⁵

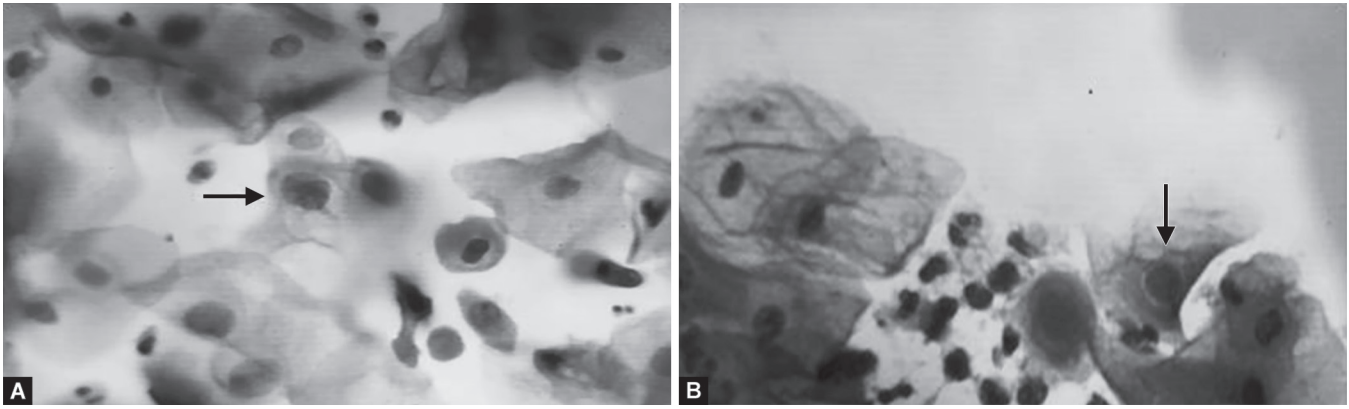
In our study, a total of 40 cases falling under the high-risk category were studied to compare the sensitivity of LBC and CP as

Table 1: Distribution of cases according to the high-risk factors

S. no.	Factors	No of cases	Percentage
1	Postcoital bleeding	2	5
2	Postmenopausal bleeding	1	2.55
3	History of early sexual activity (<18 years)	21	52.5
4	Multiple sexual partners	1	2.5
5	Multiparity	10	25
6	Clinical diagnosis of cervical erosion	05	12.5

Table 2: Distribution of cases according to the method of screening

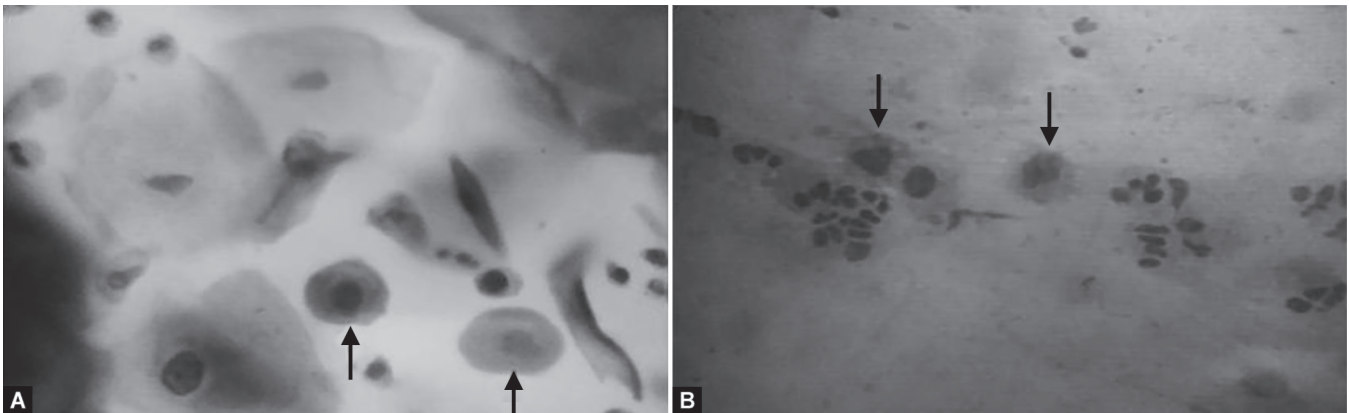
Category	No. of cases of LBC	Percentage	No. of cases of CP	Percentage	No. of common cases	
					Percentage	Percentage
NILM	29	72.5	32	80	24	77.4
ASCUS	2	5	1	2.5	1	3.2
LSIL	5	12.5	5	12.5	4	12.9
HSIL	4	10	2	5	2	6.5
TOTAL		40		40		31



Figs 1A and B: (A) Nucleomegaly and hyperchromasia in a low-grade squamous intraepithelial lesion (LBC 10× 40×); (B) Nucleomegaly, hyperchromasia, and anisonucleosis in a low-grade squamous intraepithelial lesion (CP 10× 40×)

Table 3: Cytohistological correlation and sensitivity of liquid-based cytology

Cytology		Histology					Sensitivity for detecting positive cases (%)
Category	Number of cases	Number of cases received	Normal/ inflammatory	LSIL	HSIL	Carcinoma	
NILM	29	1	1	—	—	—	100
ASCUS	2	2	—	2	—	—	100
LSIL	5	5	1	4	—	—	80
HSIL	4	4	—	2	1	1	100



Figs 2A and B: (A) Small cells with nucleomegaly, hyperchromasia, and irregular nuclear membrane in a high-grade intraepithelial lesion (LBC 10× 40×); (B) Small cells with nucleomegaly, hyperchromasia, and irregular nuclear membrane in a high-grade intraepithelial lesion (CP 10× 40×)

Table 4: Cytohistological correlation and sensitivity of a conventional PAP

Cytology		Histology					Sensitivity for detecting positive cases (%)
Category	Number of cases	Number of cases received	Normal/ inflammatory	LSIL	HSIL	Carcinoma	
NILM	32	1	1	—	—	—	100
ASCUS	1	1	—	1	—	—	100
LSIL	5	5	—	5	—	—	100
HSIL	2	2	—	1	—	1	100

a screening tool to detect abnormal cases. The age of the patients ranged from 20 to 70 years. Most of them were aged 31–40 years (35%), closely followed by 20–30 years (32.5%), similar to the studies done by Zarchi et al.¹ and Pankaj et al.⁶

Of the total cases, 21(52.5%) came with the history of early sexual activity, and 10 (25%) patients gave the history of multiparity. An estimated 5 (12.5%) patients already had the clinical diagnosis of cervical erosion; 2 (5%) complained of post coital bleeding. Only

1 (2.5%) case had the complaint of post menopausal bleeding and only 1 case (2.5%) had the history of multiple sexual partners, which could be due to the difficulty in eliciting proper history. We encountered a maximum number of cases having the history of early sexual activity. Sherwani et al.⁸ also observed that the majority of cases in their study had a history of early sexual activity, which is in agreement with our study. In contrast, Taylor et al.⁹ observed multiparity as a major high-risk factor in their study. This could be due to the fact that the study done by Sherwani et al.⁸ was done in India, where early marriage of girls is a common practice. Also the age of early sexual activity was considered to be less than 18 years in our study, whereas it was 16 years in the study done by Taylor et al.⁹

Of the 40 cases who underwent screening, 32 (80%) cases were diagnosed as negative for intraepithelial lesion/malignancy (NILM) on CP and 29 (72.5%) on LBC. A total of 24 (60%) cases were diagnosed as NILM by both the methods; 1 NILM case reported on CP and LBC each was received for histology, which was reported as normal. Thereby, the sensitivity came out to be 100% for both CP and LBC.

ASCUS was diagnosed in 1 (2.5%) case on CP and in 2 (5%) cases by LBC that means LBC identified 1 (2.5%) supplementary case of ASCUS in comparison to CP. There was only 1 (2.5%) case that was diagnosed as ASCUS by both the methods. Only one case of ASCUS reported by CP was received for histology and was reported as LSIL, giving its sensitivity as 100%. Similarly, two cases reported as ASCUS on LBC were received for histology and were reported as LSIL; therefore the sensitivity for LBC also came to be 100%. LBC detected more cases of ASCUS in comparison to CP, which is concordant with the studies done by Monsonego et al.,¹⁰ Cheung et al.,¹¹ Zheng et al.,¹² Filho et al.,¹³ who also observed the same with almost no difference in the sensitivity of both these methods. On the other hand, Luthra et al.,¹⁴ Lerma et al.,¹⁵ and Siebers et al.¹⁶ observed less number of cases on LBC while no difference was observed in the rate of detection of ASCUS by LBC and CP in the studies done by Howell et al.¹⁷ and Bernstein et al.¹⁸

LSIL was diagnosed in 5 (12.5%) cases by CP and in 5 (12.5%) cases by LBC and there were 4 (10%) cases diagnosed as LSIL by both methods. Histology of the 5 cases reported as LSIL on CP revealed LSIL on biopsy as well, giving the sensitivity as 100%. Among the five cases reported as LSIL on LBC, one was reported as chronic cervicitis with reparative changes and four were reported as LSIL on histology, giving a sensitivity of 80%, which was less than that of CP. Our result was concordant with Ilter et al.,¹⁹ who also observed more LSIL cases on CP than LBC. However Monsonego et al.,¹⁰ Cheung et al.,¹¹ Sherwani et al.,⁸ Zheng et al.¹² and Filho et al.,¹³ diagnosed more LSIL on LBC than CP.

HSIL was diagnosed in 2 (5%) cases by CP and in 4 (10%) cases by LBC, which means 2 additional cases were diagnosed as HSIL by LBC in comparison to CP. Among 2 cases of HSIL on CP, 1 was reported as LSIL and the other was reported as carcinoma on histology, giving a sensitivity of 100%. Similarly, among 4 cases of HSIL on LBC, 2 were reported as LSIL, 1 was reported as HSIL and 1 as carcinoma, giving the sensitivity as 100%. Thus, LBC detected more cases of HSIL in comparison to CP but the sensitivity of both these methods remained the same, similar to the observations of Monsonego et al.,¹⁰ Cheung et al.,¹¹ Zheng et al.,¹² and Filho et al.¹³ and Davey et al.²⁰

In our study, most of the epithelial abnormalities were equally detected by both the screening methods, with LBC being superior in detecting more ASCUS and HSIL cases when compared to CP;

however, the sensitivities of both these techniques were almost similar. Taylor et al.,⁹ Arbyn et al.,²¹ Pankaj et al.⁶ also showed similar observations with almost no significant disparity between LBC and CP as a screening technique in detecting premalignant lesions in high-risk females. Thus, our study was concordant with them.

CONCLUSION

Both the screening methods are very effective and sensitive in the detection of premalignant lesions with slight discordance of grade on histology. Thus, we conclude that cervical cytology is very effective in the detection of premalignant lesions with the sensitivity of almost 100%. Thereby, all the females above 30 years of age and showing high-risk behavior should undergo cervical screening irrespective of the method used. In developing countries such as India, where finances pose a major problem, conventional method is as good as LBC.

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