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Comparative Study of Cervical Pathology by Liquid Based Cytology and Conventional PAP in Jhalawar

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Abstract

Objective: The aim of this study is to compare the morphology of cervical lesions by Conventional pap and Liquid based cytology.

Methods: In 1.5-year prospective study, from July 2019 to December 2020, total 156 cases were analyzed. Females of age group 21 – 70 years attending Gynecology outpatient department for complain of white discharge bleeding per vagina, post coital bleeding, irregular menstruation and for routine cervical cancer screening were included. Pap smear and LBC were taken. Smears were examined after staining with Rapid Pap staining.

Result: LBC showed higher specimen adequacy, cellularity, clean background and uniform distribution of cells as compare to CPS.

Conclusion: In our study LBC showed improved adequacy, better cytomorphological features and better detection of epithelial abnormalities compared to CPS. Thus, LBC is a better tool in detecting cervical lesions than CPS.

Keywords: Liquid Based Cytology, Conventional Pap smear

Introduction

Cancer is the disease of the century and the leading cause of death around the world resulting in 13% of all causes of death in 2018. Across the globe, there are 2784 million women aged 15 years and older who are at risk of developing cervical cancer, and about 527,624 new cervical cancer cases are diagnosed annually. Cervical cancer ranks as the fourth leading cause of cancer in women worldwide, and it is the second most common cancer in women between 15 and 44 years of age. [(1,2)] Almost 70% of the global burden of cervical cancer falls in areas with lower levels of development, and more than one-fifth of all new cases are diagnosed in India. For women in India, cervical cancer is the second most common cancer. Every year in India, 122,844 women are diagnosed with cervical cancer and 67,477 die from the disease. [(3-4)] It accounts for 80% of deaths in developing countries like India. [(1,2)] Cervical cancer is also the second most common cause of cancer deaths when both genders are combined. [(5)]

Cervical cancer screening has been performed for more than 50 years by the conventional scrape smears stained by Papanicolaou (Pap) stain, which has substantially reduced the incidence of cervical cancers, especially in developed countries. However, the Pap smear has been reported to have low sensitivity.[6]

To overcome the limitations of conventional Pap smear (CPS), liquid-based cytology (LBC) was introduced in 1990s as a better tool for processing cervical samples. It is a new technique in India. The shift from CPS to LBC is because LBC provides better sample quality, reproducibility, sensitivity, and specificity, as well as the ability to perform molecular testing. More than 5,00,000 subjects have been studied with a preponderance of data indicating a significant benefit of liquid-based, thin layer technology in the detection of cervical cancer precursor lesions and in the improvement of specimen adequacy.

The present study was conducted with the aim to compare the Thin Prep Liquid-based cytology (LBC) with conventional Pap smear in Tertiary care Hospital, Jhalawar.

Aim of the Study

1. To compare the morphology of cervical lesions by Conventional pap and Liquid based cytology.
2. To assess the effectiveness and feasibility of LBC over Conventional Pap.

Materials and Methods

This prospective study was conducted at the Department of Pathology, Jhalawar Medical College and SHKBM Hospital, Jhalawar, Rajasthan by conventional Pap smear and liquid based cytology over a period of 1.5 years. In our study, we proposed to compare Conventional PAP with the new method Liquid based cytology. The study was conducted on 156 patients selected randomly from patients coming to outpatient department of Obstetrics and Gynecology, SHKBM Hospital, Jhalawar, Rajasthan.

Cervical cytology samples from all women from 21 – 70 years attended obstetrics and gynecology outpatient department with presenting complaints of white discharge per vagina, bleeding per vagina, post coital bleeding, irregular menstruation and for routine cervical cancer screening were included in our study. Non co-operative patients, patients who do not give consent, patients with massive bleeding PV, pregnant women, patients with total hysterectomy with the removal of cervix, women without cervix were excluded.

After obtaining proper consent, proforma was given to each patient and detailed history was obtained.

For obtaining the sample, first for Conventional PAP, Ayre's spatula/endocervical brush was inserted into the cervix and gently rotated in clockwise fashion at 360 degree. Then, sample was smeared onto a grease free slide and fixed in alcohol. After fixation, smear was stained with the Rapid PAP stain.

For Liquid based cytology, Cervex brush issued by the manufacturer was introduced in such a way that central bristles go into the endocervical canal and lateral bristles placed against the ectocervix and rotated clockwise by 360 degrees for 8-10 times. Then, the brush head is rinsed vigorously in Presevcyt transport medium in vial which contains fixative issued by the manufacturer for transport. The vial is capped, labelled and taken to laboratory for slide preparation. At the laboratory, the vial is placed into the ThinPrep 2000 Processor. Cells are separated from suspension by filtration and deposited on the slide in a circular area of 20 mm diameter by controlled pressure. Slides are stained with Rapid Pap method.The PAP smears and the LBC slides were examined and recent 2014

Bethesda system of classification were used for reporting. Both the reports were correlated.

Statistical analysis

The results obtained were subjected to SPSS version 20.0.

Results and Observation

In our study, maximum number of patients who were screened was in the fourth decade of life. On observing CPS and LBC, maximum patients show NILM, followed by LSIL, ASCUS and HSIL. 7 unsatisfactory smears were reported by means of CPS while no unsatisfactory smear was reported by LBC. About 30.13% presented with white discharge per vaginum, followed by 28.21% patients with irregular bleeding, 21.15% with lower abdominal pain, 16.67% with bleeding P/V, 2.56% came for routine examination and 1.28% showed post coital bleeding. So, the most common presenting complaint was white discharge. LSIL were observed to be more 8.33% in LBC than 5.77% in PAP. HSIL was more in PAP (1.28%) than 0.64% in LBC. LBC detected one case of carcinoma whereas none was detected in CP. Chi square statistical analysis was done to observe intergroup comparison between PAP and LBC, and a statistically significant difference (p-value<0.05) was observed between both.

Table 1: shows age wise distribution of cases (LBC). Maximum number of patients was observed in age group of 36-40yrs and minimum number of patients was of age 21-25yrs. On observing LBC smear, maximum patients show NILM, followed by LSIL, ASCUS and HSIL. One case of carcinoma was detected with no unsatisfactory smear.

Table 2 shows case distribution according to presenting complaint. 30.13% shows white discharge, followed by 28.21% patients with irregular bleeding, 21.15% with lower abdominal pain, 16.67% with bleeding P/V, 2.56% came for routine examination and 1.28% showed post coital bleeding.

Table 3 shows the comparison of PAP and LBC results. PAP shows 7 unsatisfactory smears, whereas LBC shows no unsatisfactory smear. NILM was observed to be more in LBC (88.46%) than PAP (86.53%). ASCUS was same in both PAP and LBC groups. LSIL were observed to be more 8.33% in LBC than 5.77% in PAP. HSIL was more in PAP (1.28%) than 0.64% in LBC. Carcinoma was observed only in LBC in one smear. Chi square statistical analysis was done to observe intergroup comparison between PAP and LBC, and a statistically significant difference (p-value<0.05) was observed between both

Table 4 shows comparison of cytological findings by Conventional PAP smear & Liquid based cytology. We observed 7 unsatisfactory smears in case of Conventional PAP, showing a statistically significant relation between PAP and LBC.

Table 1: Age Wise Distribution of Cases (LBC)

Age	Unsatisfactory	NILM	ASCUS	LSIL	HSIL	Carcinoma
21-25	0	5	0	0	0	0
26-30	0	9	0	0	0	0
31-35	0	14	1	0	0	0

36-40	0	35	0	2	0	0
41-45	0	27	0	3	0	0
46-50	0	25	1	4	0	0
51-55	0	5	0	1	0	1
56-60	0	10	0	1	0	0
>60	0	8	1	2	1	0
Total	0	138	3	13	1	1

Table 2: Case Distribution according to presenting complaint

Complaints	No. of cases	Percentage
White discharge P/V	47	30.13
Irregular menstrual bleeding	44	28.21
Lower abdominal pain	33	21.15
Bleeding P/V	26	16.67
Routine Examination	4	2.56
Post coital bleeding	2	1.28

Table 3: Comparison of PAP and LBC results

Category	PAP (number)	PAP (%)	LBC (number)	LBC (%)
Unsatisfactory	7	4.48	0	0
NILM	135	86.53	138	88.46
ASCUS	3	1.93	3	1.92
LSIL	9	5.77	13	8.33
HSIL	2	1.28	1	0.64
Carcinoma	0	0	1	0.64
Total	156	100	156	100
CHI Square	12.187			
P-Value	<0.05			

Table 4: Comparison of Cytological findings by Conventional PAP smear & Liquid based cytology

Category	PAP (number)	PAP (%)	LBC (number)	LBC (%)	P value
Unsatisfactory	7	4.48	0	0	<0.05
NILM	135	86.53	138	88.46	
Normal	39	25	45	28.85	
Inflammatory	84	53.85	77	49.35	<0.05
Atrophy	4	2.56	8	5.12	
Bacterial Vaginosis	8	5.12	8	5.12	

Epithelial cell abnormalities	14	8.97	18	11.53	>0.05
ASCUS	3	1.92	3	1.92	
LSIL	9	5.77	13	8.33	
HSIL	2	1.28	1	0.64	
Carcinoma	0	0	1	0.64	
Total	156	100	156	100	

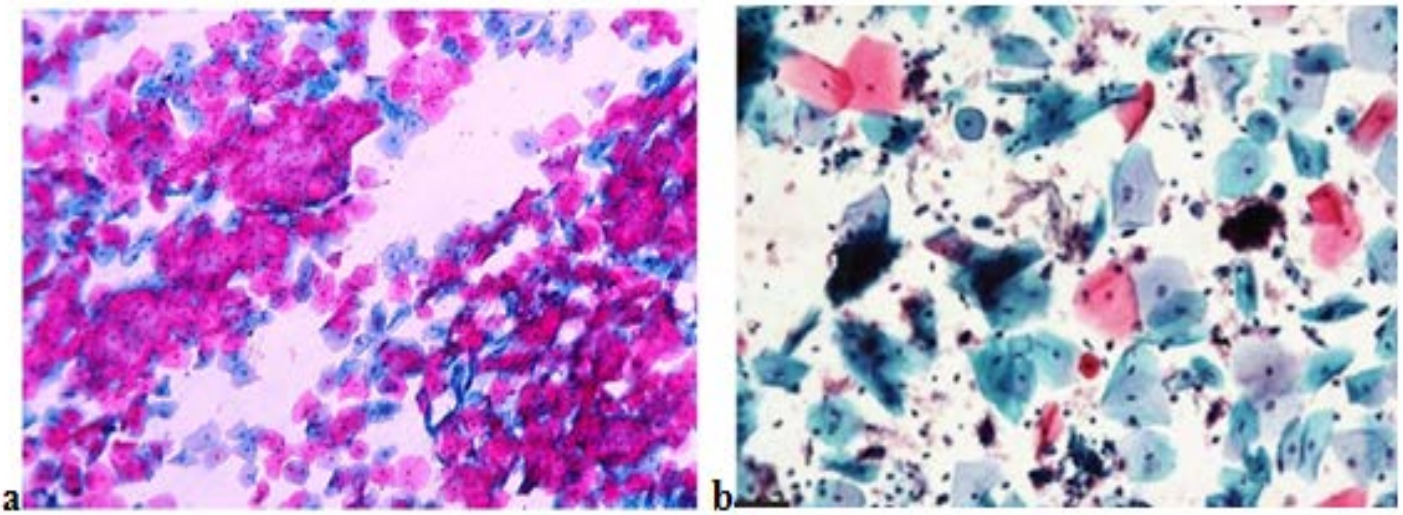

Figure 1: Satisfactory smear :(a) CPS -Smear showing approximately 100 cells. Cellularity of whole slide is >8000. (b)LBC- Smear shows admixture of superficial and intermediate squamous cells. Superficial cells have small condensed nuclei.

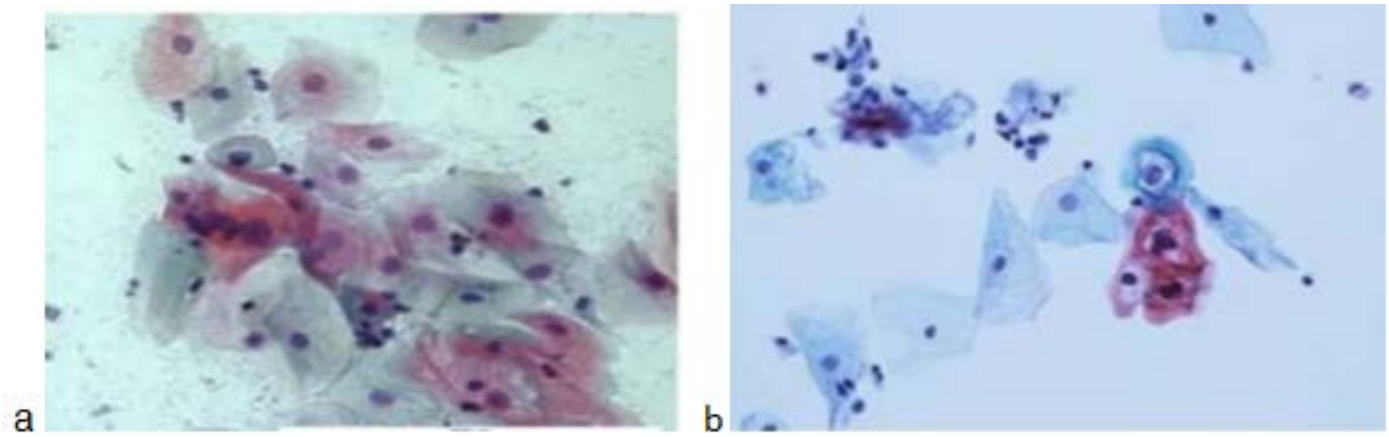

Figure 2: ASCUS: (a) CPS- Smear shows atypical squamous cells with orangeophilic cytoplasm (Atypical parakeratosis). (b) LBC- Koilocytes showing well defined perinuclear clearing and mild nuclear abnormalities.

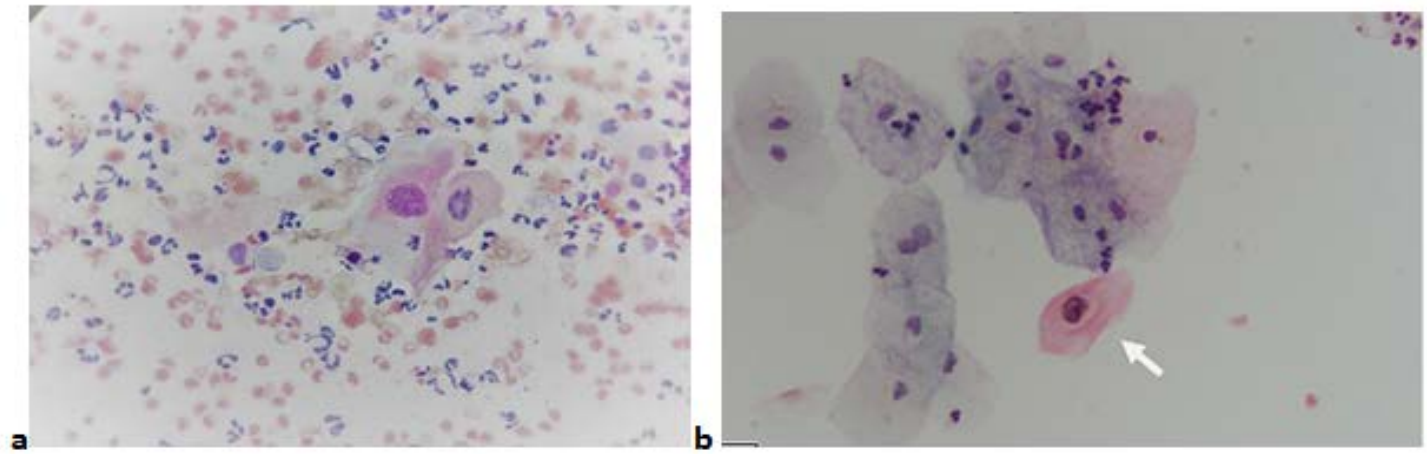

Figure 3: LSIL:(a) CPS- Smear showing mature squamous cells with enlarged nuclei with variable chromatin and nuclear membrane. (b) LBC-Smear showing an atypical large squamous cell. The atypical cell has a nucleus greater than three times the size of an intermediate squamous cell. It also shows koilocytic change (arrow).

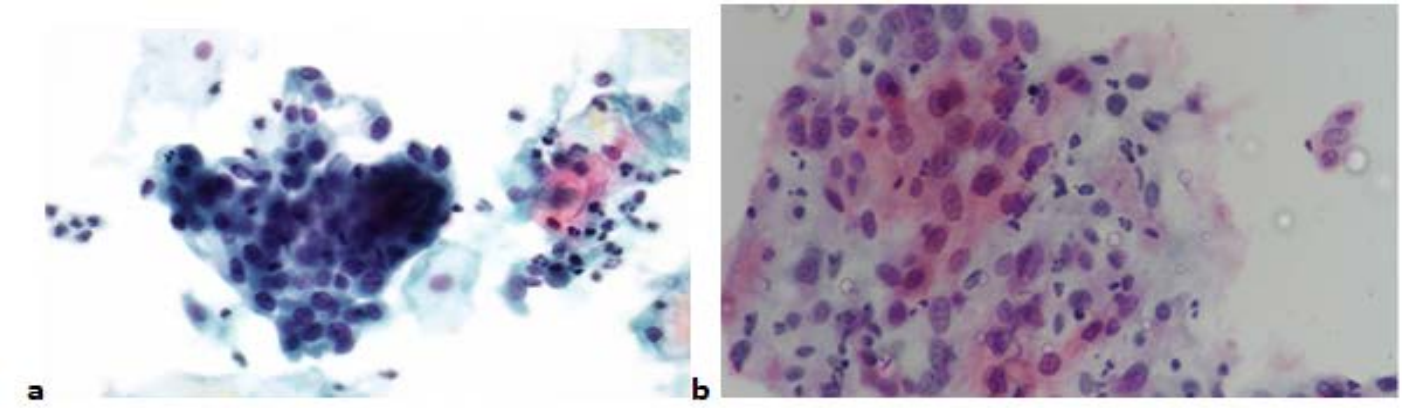

Figure 4: High grade squamous intraepithelial lesion (HSIL):(a) CPS-Smear showing features of dysplasia including significant nuclear size variation admixed with inflammation. (b) LBC - Smear showing syncytial like aggregates of atypical squamous cells with marked atypia.

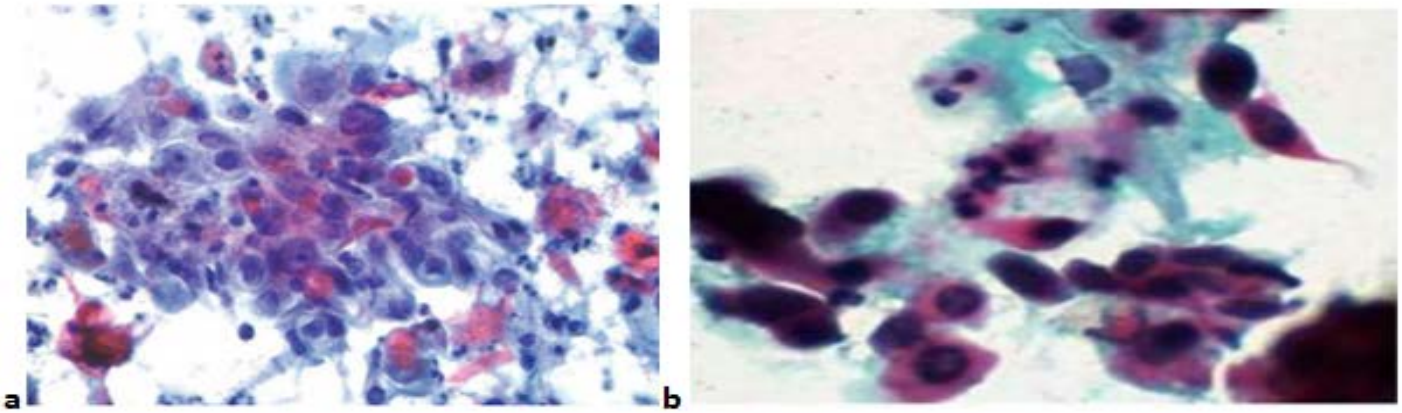

Figure 5: Squamous cell carcinoma (Keratinizing): (a)CPS– Smear showing marked pleomorphism of cells and shape, cytoplasmic keratinization and tumour diathesis in the background. (b) LBC (ThinPrep)-

Smear showing abnormal keratinized cells and spindle cells.

Discussion

This study was conducted with the aim to compare the ThinPrep Liquid-based cytology (LBC) with conventional Pap smear in Tertiary care hospital, Jhalawar.

In this study, maximum number of patients was observed in age group of 36-40yrs. Similar findings were observed in study by Sherwani RK et al., [7] who found that 77 (48.1%) cases studied belonged to fourth decade of life, followed by 50 (31.2%) cases in the third decade.

In our study, on observing conventional pap smear and LBC, maximum patients show NILM, followed by LSIL, ASCUS and HSIL. No carcinoma was detected and 7 unsatisfactory smears were reported by CPS. On observing LBC one case of carcinoma was detected with no unsatisfactory smear.

Similar findings were observed in study by Pankaj S et al [8] whose Unsatisfactory rate of CPS in our study was 7.1% and it was 1.61% for LBC, and this difference is statistically significant. Similar result is noticed in many previous studies.[9] LBC leads to almost complete elimination of most of the causes for unsatisfactory conventional preparation, with scant cellularity remaining as the main cause for unsatisfactory LBC. In a study by Singh VB et al. [10], 4.3% smears were reported as unsatisfactory by conventional method and 1.7% smears unsatisfactory by LBC technique.

In this study, we observed that 30.13% showed white discharge, followed by irregular bleeding, lower abdominal pain, bleeding P/V, and 1.28% showed post coital bleeding.

In study by Singh S et al. [11], most common presenting complaint was white discharge per vagina (40%). Similar finding was observed by Sherwani RK et al. [7], they also found that most common presenting complaints in their study was white discharge per vagina, in (42.5%) cases. Kenneth et al. [12], have emphasized the significance of vaginal discharge and its association with neoplastic changes in the cervix. These finding was also observed in our study, i.e., patients presenting with complaints of white discharge were associated with neoplastic lesions in cervix. Aboobacker KK et al. [13] also reported that Women presented with complaints of white discharge per vaginum (19%), bleeding per vagina (15%), dysfunctional uterine bleeding (2.9%), pain in abdomen (4.6%), prolapsed (6.7%), burning micturition (0.8%) or came for routine check-up (50.8%).

Our finding is in discordance with the study of Karimi-Zarchi M et al. [13] who reported most common presenting complaint was post-menopausal bleeding in 30.7%.

In our study, PAP shows 7 unsatisfactory smears, whereas LBC shows no unsatisfactory smears. NILM was observed to be more in LBC (88.46%) than PAP (86.53%). ASCUS was same in both PAP and LBC groups. LSIL were observed to be more 8.33% in LBC than 5.77% in PAP. HSIL was more in PAP (1.28%) than 0.64% in LBC. Carcinoma was observed only in LBC in one smear. Chi square statistical analysis was done to observe intergroup comparison between PAP and LBC, and a statistically significant difference (p-value<0.05) was observed between both.

Similar results were obtained in study by Singh U et al. [14], and Aboobacker KK et al. [13], also showed similar distribution of identification of cells in both smears. They also revealed that the comparison of cytological findings of conventional Pap smear and LBC. Significant number of negative for malignancy cells

were reported by LBC compared to conventional Pap (P<0.001).

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 behaviour should undergo cervical screening irrespective of the method used. LBC can be a better alternative to conventional smear because of lower rate of unsatisfactory smears.

Results showed that the LBC method may improve the sample's quality and reduce the number of unsatisfactory cases more than the conventional CP method. However, as the detection rate of epithelial abnormalities is better with LBC techniques. CPS is still the best screening method in the Indian scenario with a low-resource setting considering its cost-effectiveness over LBC.

Conclusion

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 behaviour should undergo cervical screening irrespective of the method used. LBC can be a better alternative to conventional smear because of lower rate of unsatisfactory smears.

In our study LBC showed improved adequacy, better cytomorphological features and better detection of epithelial abnormalities compared to CPS. Thus, LBC is a better tool in detecting cervical lesions than CPS. Furthermore, residual LBC sample is available to perform HPV DNA testing. LBC with concomitant HPV testing can prove to be more effective in high resource setting.

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