Cervical cancer screening by conventional Pap smear versus liquid based cytology

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ABSTRACT

Aims: To evaluate Liquid Based Cytology (LBC) diagnostic performance compared with Conventional Pap Smear (CPS) for cervical cancer screening and to compare the sensitivity and specificity of the two cytology methods with gold standard cervical biopsy.

Methods: This is a hospital based cross-sectional study conducted from April 2017 to April 2018 in 110 sample randomly selected at gynecology OPD in Paropakar Maternity and Women's Hospital. Paired samples (CPS and LBC) were taken from the same patient. Abnormal epithelial lesion detected in LBC and CPS was sent for biopsy. Bethedsa reporting system was followed and data analyzed in terms of diagnostic accuracy.

Results: LBC vs CPS for satisfactory report was 96.4% vs 91.8% while unsatisfactory was 3.6% vs 1.8% (p=0.02). The detection of premalignant lesions was ASCUS 2.7%, HSIL 4.5%, ASCUS-H 1.8% and LSIL 0.9% by LBC while by CPS- ASC-US 0.9%, HSIL 3.6%, LSIL 1.8% and ASC-H 0.9% were detected. The sensitivity and specificity of LBC vs CPS was 100% vs 88% and 81.8% vs 99% respectively. The positive predictive and negative predictive value of LBC vs CPS was 81.8% vs 88% and 100% vs 99% respectively.

Conclusions: Cell pick-up was satisfactory in both LBC and CPS. The sensitivity and positive predictive value of CPS is similar whereas the positive predictive value of LBC is less than its sensitivity. Cervical cancer screening with CPS is effective alternative over LBC by its cost and level of accuracy.

Key words: cervical cancer screening, conventional Pap smear, liquid based cytology

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INTRODUCTION

Globally, 528000 new cases of cancers are reported every year and 266000 die of cervical cancer. It is the fourth most common cause of cancer death.[1] In Nepal, 3372 cases (29%) are cervical cancer among total of 11469 cases with 1100 annual deaths. Cervical cancer is among the top 10 cancers and number one among the women in Nepal.[2,3]

Generally, the progression to invasive cancer is slow and has a predictable pattern. In longitudinal studies 30-70% of untreated patients with precancer will develop invasive carcinoma in 10-12 years while only 10% of lesions progress to invasive carcinoma in less than one year.[4]

Epidemiological data have indicated that organized screening with Pap smear leads to reduction of incidence of carcinoma by 75% but its sensitivity reduces to less than 50% when there is presence of obscuring blood, inflammation or thick areas of overlapping epithelial cells.[5] These problems with the CPS, gave rise to the advanced technology of Liquid Based Cytology (LBC) like "Thin Prep" and "Sure Path™".[6]

Unfortunately, many women fail to comply with screening recommendations. Patient's ignorance of guidelines, dislike of pelvic examination, lack of access to the medical care system, fear of cancer, fear of pain from diagnostic procedures, and mistrust of medical authorities are the considered reasons.[7]

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In low resources area where LBC is not possible CPS is equally effective and viable tool for screening. Hence the objective of the study is to compare the diagnostic performance of LBC compared with CPS for cervical cancer screening.

METHODS

A cross-sectional study was conducted in Paropakar Maternity and Women's Hospital (PMWH) from April 2017 to April 2018 following ethical approval. Paired samples were obtained by convenience sampling of 110 patients were taken that were randomly selected from gynecology outpatient department.

Patients from age group 21-65 years, non-pregnant, and any abnormal findings in the speculum were included in the study. Previously screened cases, hysterectomy or surgeries related to cervix like Fothergill's and trachelectomy were excluded.

Paired samples were taken from the same patient. Initially, sample for conventional Pap smear (CPS) was taken using an Ayer's spatula, thin smear prepared and immediately immersed in 95% ethanol in Coplin jar prepared for conventional Pap staining. In the same single sitting second sample was collected in a vial containing 10 ml of SurePath™ preservative for LBC using the detachable cervical brush. Samples were taken from endocervix as well as ectocervix. The brush was completely rotated at 360° five times. The sample for Pap smear was coded with number and alphabet while Pap smear sample was numerically coded. Samples were processed using the Tripath machine.

Bethesda system of reporting was adopted. Nine parameters were compared between the two techniques that included cellularity, background, uniform distribution, artifact, cellular overlapping, architectural, cellular morphological change, nuclear changes, and inflammatory infiltrate. Two week after the screening test the histopathology was sent from the lesion diagnosed as HSIL, LSIL, ASC-US and ASC-H. Biopsy report with cervical intra epithelial lesion I, II, III and cervical cancer were considered positive; date entered in statistical software SPSS 16; and Chi-square test was applied. Sensitivity and specificity of the two tests were compared.

RESULTS

Among the 110 participants they were under age group between 21-55 years and maximum were of 31-40 years (44.5%); 76.4% belonged to the rural area but migrant to Kathmandu; 66.3% were 16-20 years of age; 87.3% had single partner; 30% smoker; and contraception was used by 62.8% [Table-1].

Table-1: Socio-demographic characteristics

	Age in years	N	%
Age distribution	21-30	27	24.5%
	31-40	49	44.5%
	41-50	31	28%
	51-60	03	2.7%
Age of sexual activity	<15	12	10.9
	16-20	73	66.3
	21-25	21	19

There were more cellular overlapping, unclean background and artifacts in conventional Pap than in LBC; but the cellular adequacy and pick-up of endocervical cells were similar to both techniques [Table-2].

Table-2: Morphological Features between CPS and LBC Methods

Morphological Features	*LBC (%)	*CPS (%)
Adequate cellularity	108 (98.2)	104 (94.5)
Endo-cervical	101 (91.8)	102 (92.7)
Cellular overlapping	13 (11.8)	106 (96.4)
Unclean background	23 (20.9)	107 (97.3)
Artifacts	27 (24.5)	94 (85.5)
Architectural change	7 (6.4)	98 (89.1)
Cellular morphological change	7 (6.4)	105 (95.5)
Nuclear change	15 (13.6)	92 (83.6)
Uniformity of distributions	107 (97.3)	75 (68.2)

**LBC: Liquid based cytology, CPS: Conventional Pap smear*

Following the Bethesda System, the cytological report in LBC and CPS were comparable in terms of satisfactory smear to report, detection of precancer and reactive conditions (p=0.02) [Table -3].

Eight out of 9 precancer lesions detected by CPS were verified by biopsy whereas 9 out of 11 precancer detected by LBC were biopsy proven. The sensitivity and positive predictive value of CPS is similar whereas the positive predictive value of LBC is less than its sensitivity [Table-4].

DISCUSSION

The performance of LBC and CPS were compared with regard to its detection and diagnostic performance. This study was done in a small group of population who were enrolled for the first time in the screening program. Same person were applied with both cytological test using two different tool separately (Ayre's spatula and cytobrush). The method of exfoliating the cells differed from other studies.[5,8,9,] Because of the variation in the application technique the cells extracted were adequate and endocervical cells were adequately picked up. There was high yield of satisfactory and less unsatisfactory report in both LBC and CPS which was contradictory to other studies.[5, 10-12]

The detection of ASC-US, ASC-H, HSIL AND LSIL were similar to some studies [8.11,13] but low compared to others.[5,10] The variations in the feasibilities in the success rate of detecting the precancerous cervical lesions was probably due to the differences in the sample size between my study and other studies. The studies done by Karimi Zarichi et al[10] and Macharia et al[9] were from previously screened cases of abnormal Pap smear while the participants in my study were screened for the first time.

Screening has played a major role in detection and reduction of death from cervical cancer with timely intervention. In the area with high number of ignorant or lost to follow up cases sometimes it is important to apply screen and treat method. This could cause overtreatment but this would prevent high risk of disease progression and presentation in advanced stage. For this the test has to be highly specific and have high negative predictive value.

The sensitivity and specificity of the LBC in this study was 100% vs 81.8%which was comparable to studies.[9,14,15] The sensitivity of CPS in this study was 88% highest when compared to other studies.[5,9,10,15]

The specificity of CPS of this study was 99% similar to Dhananjaya et al.[14] The results were superior when compared with study.[5,9,10] From our result as both the test have high specificity and negative predictive value; and CPS has similar sensitivity and positive predictive value we can prefer CPS whenever LBC is not available.

Table-3: Comparison of CPS and LBC by Bethesda reporting system

Parameters	LBC (%)	CPS (%)
Satisfactory	106 (96.4)	101 (91.8)
Inflammation (reactive)	43 (39)	43(39)
Unsatisfactory	4 (3.6)	9 (8)
Trichomonas vaginalis	3 (2.7)	2 (1.8)
Bacterial vaginosis	8 (7.3)	7 (6.3)
Atrophy	1 (0.9)	1 (0.9)
ASC-US	3 (2.7)	2(1.8)
ASC-H	2 (1.8)	1 (0.9)
LSIL	1 (0.9%)	2 (1.8%)
HSIL	5 (4.5%)	4 (3.6%)

Table-4: Sensitivity and Specificity of CPS and LBC

	Sensitivity	Specificity	PPV	NPV
CPS	88%	99%	88%	99%
LBC	100%	81.8%	81.8%	100%

The limitations of the study are shorter duration of study and smaller sample size. Result verification biopsy was not free of sampling bias as it was not colposcopy guided procedure.

CONCLUSIONS

Cell pick-up was satisfactory in both LBC and CPS. The sensitivity and positive predictive value of CPS is similar whereas the positive predictive value of LBC is less than its sensitivity. Cervical cancer screening with CPS seems effective alternative over LBC by its cost and level of accuracy.

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