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COMPARISON OF LIQUID BASED CYTOLOGY WITH CONVENTIONAL PAPANICOLAOU METHOD IN SCREENING OF PAP SMEARS

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Abstract:

Background: Cervical cancer is the 2nd most common cancer in women worldwide and the most common cause of death in the developing countries. However, cervical cancer can be prevented if dysplastic changes are detected early. Conventional Papanicolaou cytology has been the mainstay for cervical cancer screening but it has many limitations. To overcome these limitations, liquid based cytology was introduced.

Aims & Objectives: The aim of the study is to assess the utility of Liquid Based Cytology (LBC) in comparison to conventional Papanicolaou (PAP) smears.

Material & Methods: The present study was carried out in 100 cases. A comparison was done between both conventional Papanicolaou cytology and liquid based cytology. It was a double blind study so as to prevent interpretative bias. Only one experienced cytopathologist interpreted all cytology slides so that no interpersonal variation could interfere with the result.

Results: Inflammatory smears on liquid based cytology and conventional cytology were 25% and 63% respectively only 2% cases of specific infection were detected on conventional cytology as compared to 12% cases on liquid based cytology. There was a significant difference in the reporting rate of Low-grade squamous cell carcinoma (LGSIL), 6% were found to have LGSIL on liquid based cytology whereas only 3% were reported on conventional cytology. Similarly, atypical squamous cells of undetermined significance (ASCUS) were reported in 3% cases on liquid based cytology as compared to only 1% case on conventional cytology.

Conclusion: An array of lesions can be potentially diagnosed on Liquid based cytology. Proper technique is essential for proper interpretation and diagnosis. This can lead to a reduction in number of inadequate smears and improve the smear quality.

Keywords: Atypical squamous cells of undetermined significance, Conventional Papanicolaou Cytology, Liquid based cytology, Low grade squamous cell changes.

INTRODUCTION

In India, Cervical cancer is the most common cancer in females and the second most common cancer worldwide. Early detection of cervical cellular changes and cervical intraepithelial neoplasia (CIN) followed by appropriate treatment reduces the risk of developing cancer [1]. The conventional Papanicolaou test, developed by the Greek doctor George Papanicolaou in 1941 as a tool for early detection of cervical cancer is commonly used in control programs of cervical cancer. However it has high rates of false negativity [2].

In 1990's LBC was developed and approved in 1996 by the United States Food and Drug Administration. LBC was introduced to improve sensitivity because it permits the use of a monolayer of cells to facilitate the diagnosis[3].

Two FDA approved methodologies of LBC widely used are Thin Prep & SurePath. Another method of performing LBC is Manual liquid based cytology called as Liqui-Prep. This system includes a chemical vial in which the cells are preserved, a standard laboratory centrifuge and a special chemical solution that acts as a membrane matrix [4]. Liqui-Prep is however not yet approved by FDA.

MATERIAL AND METHODS

The present study was conducted in the Department of Pathology, D.Y. Patil University

School of Medicine, Nerul, Navi Mumbai over a period of 2 years from November 2015 to November 2017. The study was conducted on a total of 100 cases. The present study included all consenting adult women who came to obstetric and gynecological outpatient department and were advised PAP smear. Post-hysterectomy patients and treated cervical carcinoma cases were excluded from the study. Written informed consent of each patient were obtained after explaining the details of the study

Conventional Papanicolaou cytology and Liquid based cytology were performed as per the protocol. Conventional Papanicolaou slides and liquid based cytology slides were then coded. Experienced Cytopathologist was unaware of the coding system so as to avoid any interpersonal bias and the slides were reported according to the Bethesda system 2014.

Statistical Analysis

Results of both the conventional method and the liquid based cytology were compared and statistically analysed by chi-square test.

RESULTS:

Out of 100 cases, all the cases were adequate for reporting on liquid based cytology whereas 97 cases were adequate and 3 cases were inadequate for reporting on conventional Papanicolaou cytology.

Of the 100 patients, 11 patients (11%) belonged to the age group of 20-30, 35 (35%) patients belonged to the age group 31- 40, 43 (43%) patients belonged to the age group of 41-50, 6 (6%) patients belonged to 51-60 age group and 5 (5%) belonged to more than 60 years of age as shown in table 1. In our study, maximum number of cases of squamous cell changes was found in the 4th decade of life.

Table 1: Distribution of cases according to the age group.

Age Group	No of Cases	Percentage (%)
20-30	11	11
31-40	35	35
41-50	43	43
51-60	6	6
>60	5	5
Total	100	100

Table 2 depicts the clinical presentation of the 100 cases, it can be seen that maximum number of patients presented with irregular menstruation in our study.

Table 2: Distribution according to clinical presentation

Presenting Symptoms	No of Cases	Percentage (%)
PV discharge	14	14
Menstrual Irregularity	37	37
Abdominal pain	17	17
PV Bleeding	5	5
Others	27	27
Total	100	100

In our study, out of 100 cases, 90 were reported as negative for intraepithelial lesion or malignancy on conventional PAP smear in contrast to 87 cases on liquid based cytology. This category of NILM included Normal smear, inflammatory smear, Menopausal atrophic smear, Squamous metaplasia, Bacterial vaginosis, Trichomonas vaginalis & Candidiais. 7 cases were found to have squamous cell changes on conventional PAP smear however, 13 cases were reported with squamous cell changes on liquid based cytology. Squamous cell changes included ASCUS, ASC-H, LGSIL and HGSIL. 3 cases were inadequate for opinion on conventional PAP due to inadequate cellularity as depicted in table 3.

Table 3: Distribution of cases into type lesion

Lesion	Conventional PAP	LBC
NILM	90	87
Squamous cell changes	7	13
Inadequate for opinion	3	0
Total	100	100
p Values calculate by Chi-Square Test 0.088 (NS)		

Table 4 depicts the comparison of the diagnosis of cases which were negative for intraepithelial lesion or malignancy. 25 cases were reported as normal smear on conventional PAP as compared to 44 cases which were found to be normal on liquid based cytology. 4 cases and 2 cases were reported to be menopausal atrophic and squamous metaplastic respectively on liquid based cytology. Inflammatory smears were found to be 63 on conventional PAP whereas 25 on liquid based cytology. Bacterial vaginosis was detected in 2 cases on conventional PAP whereas 8 cases on liquid based cytology. 1 case each of Trichomonas vaginalis and Candidiasis were reported

on liquid based cytology as can be seen in figure 1. P value being significant 0.001.

Table 4: Comparison of diagnosis NILM on Conventional PAP and liquid based cytology.

Categories	Conventional PAP	Percentage (%)	LBC	Percentage (%)
Normal smear	25	25	44	44
Menopausal atrophic	0	0	4	4
Squamous metaplasia	0	0	2	2
Inflammatory	63	63	25	25
Bacterial Vaginosis	2	2	8	8
Trichomonas Vaginalis	0	0	1	1
Candidiasis	0	0	3	3
Total	90	90	87	87
p Values calculate by Chi-Square Test 0.001 (S)				

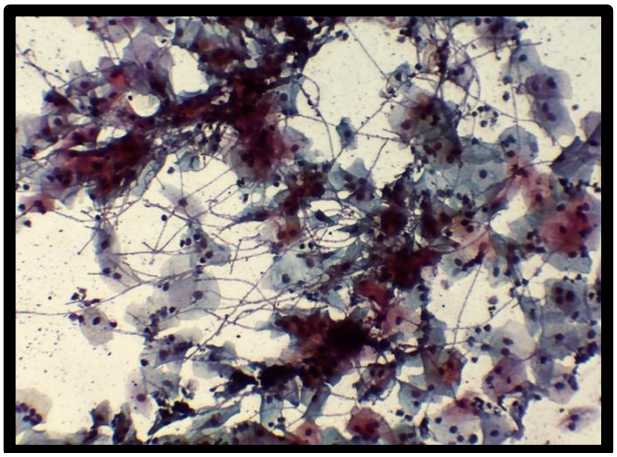

Figure 1: Pap, 40X, Candida species displaying pseudohyphae on LBC.

As illustrated in Table 5, 1 case of ASCUS was reported on Conventional PAP in comparison to 3 cases of ASCUS on liquid based cytology. Conventional PAP showed 1 case of ASC-H whereas 2 cases were reported as ASC-H on liquid based cytology. As can be seen only 3 cases were reported as LGSIL on Conventional PAP whereas 6 cases were reported as LGSIL on liquid based cytology. 2 cases were diagnosed as HGSIL on both Conventional and liquid based preparation. P value being significant 0.001.

Table 5: Comparison of diagnosis Squamous cell changes on Conventional PAP and liquid based cytology.

Categories	Conventional PAP	Percentage (%)	LBC	Percentage (%)
ASCUS	1	1	3	3
ASC-H	1	1	2	2
LGSIL	3	3	6	6
HGSIL	2	2	2	2
Total	7	7	13	13
p Values calculate by Chi-Square Test 0.001 (S)				

DISCUSSION

The conventional Papanicolaou smear has been the mainstay of screening for cervical cancer and its precursor lesions for approximately 50 years. Despite its success as a preventive screening tool for cervical cancer, conventional Papanicolaou smear has its limitations.

False negatives of the conventional Papanicolaou smear may be related to inadequate sampling, inadequate transfer of the sample onto the glass slide or deficiencies in the microscopic assessment of the slide[5]. To overcome these problems, a new slide preparation method namely the manual liquid based cytology was introduced [5]. Liquid based cytology represents a significant advantage over conventional method in terms of total cell component availability. Many studies have shown that, with proper training, manual liquid based cytology results in a higher diagnostic yield [6, 7]. In our study, manual liquid based cytology method was found to be comparable to the conventional PAP smear on some parameters and superior on others.

In the present study, 43% patients were in 41-50 years age group. Minimum age of patient screened was 23 years and maximum was 81 years. Mean age of women were 42.2. This is comparable to the study by Canda et al[8] in which mean age was 39.2 years. Khaniki et al [9], in their study reported 38 years as the mean age. Park et al [10] in their study found 38.8 years to be the mean age of women enrolled in the study.

Most common presenting complaint in our study was menstrual irregularity in 37% cases followed by abdominal pain in 17% cases, discharge per vaginum in 14% cases and 5% cases presented with per vaginum bleeding.

In a study done by Sherwani RK et al [11], most common presenting complaint was found to be

discharge per vaginum in 42.5% cases, followed by pain abdomen in 27.5% cases and menstrual irregularity in 23.8% cases. Kenneth and Yao et al [12] had emphasized on the significance of discharge per vaginum and its association with neoplastic changes in the cervix. Sherwani RK et al [11] and Patidar et al [13] in their study also found discharge per vaginum as the most common presenting complaint.

In our study the number of unsatisfactory smears by conventional Papanicolaou smear was 3% whereas liquid based cytology did not show any unsatisfactory smear. Our results were comparable to the study done by Ranjana et al[14] who reported 5.6% unsatisfactory smears by conventional cytology and 0.3% by liquid based cytology technique. Nandini NM et al[15] in their study found 9% unsatisfactory smears on conventional Papanicolaou cytology as compared to 1% unsatisfactory smears on liquid based cytology.

In our study, we reported 63% cases as inflammatory on conventional smear as compared to 25% cases on liquid based cytology. Garg et al [16] reported 85.5% and 46.5% cases of inflammatory smear on conventional and liquid based cytology respectively. Haghighi et al [17] also showed similar findings in their study.

In the present study we found 12 lesions of infectious diseases on liquid based cytology comprising of 8 cases of bacterial vaginosis, 1 case of Trichomonas vaginalis and 3 cases of Candidiasis whereas only 2 cases of Bacterial vaginosis were reported on conventional Pap smear. This was in concordance with the study done by Verma et al [18]. Sherwani RK et al [11] in their study reported 8.7% cases of infectious agents on liquid based cytology and 3.1% cases on conventional Pap smear.

In the present study, 13% cases were diagnosed to have epithelial cell abnormalities on liquid based cytology whereas only 7% were diagnosed on conventional Papanicolaou smears. Park et al [10] reported 8.6% and 3.7% cases with epithelial cell abnormalities on liquid based and conventional cytology respectively. Deshou et al [19,] Verma et al [18] also had concordant findings in their study.

In the present study, 1 case was reported as ASCUS by conventional method whereas 3 cases were found to be ASCUS on liquid based cytology. This finding was comparable to the study done by Park et al [10] who found 2.8% cases of ASCUS by conventional method in comparison to 6.5% cases of ASCUS on liquid based cytology. Similar findings were found in the study conducted by Verma et al [18] and Maksem JA et al [5].

In the present study 1% ASC-H was diagnosed on conventional method whereas 2% were diagnosed on liquid based cytology. Similar findings were reported in the study conducted by Deshou et al [19] and Park et al [10]

In our study, liquid based cytology showed a two-fold improvement in the detection of LGSIL as compared to a similar patient population tested with conventional Papanicolaou smear. This is comparable to the study done by Park et al [10], Maksem JA [5] and Baker J et al [20].

We found 2% cases of HGSIL on both conventional and liquid based cytology. NM Nandini et al [15] and M Tunc Canda [8] et al, in their study too found equal number of cases on both conventional and liquid based preparation. Park et al [10] and Verma et al [18] in their study showed slightly increased number of cases of HGSIL on liquid based cytology as compared to conventional smear.

CONCLUSION:

The sensitivity of liquid based cytology over routine conventional Papanicolaou smears has been statistically validated in our study across a wide spectrum of lesions. Hence, liquid based cytology is strongly advocated in the best interest of public health, by improving the quality of the sample and reducing the likelihood of false negative cytology results. Thus, it will significantly improve early detection and treatment of cervical cancer. Being economical and non-invasive method of cervical screening, the liquid based cytology when performed under standard protocol and good clinical correlation will go a long way in reducing patient morbidity and mortality.

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