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Conventional Papsmear And Liquid Based Cytology For Cervical Cancer Screening: A Comparative Study.

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ABSTRACT

To assess the sensitivity and specificity of conventional papsmear and liquid based cytology for cervical cancer screening. This comparative study was conducted on 300 patients attending the inpatient and outpatient department of gynecology in Shri balaji medical college and hospital from January 2020 - January 2021. Patients will be from age group of 21 to 65 yrs. Bleeding per vaginum during the visit Pregnant women Uncooperative patients Treated cervical cancer cases. In this study both liquid based cytology and conventional pap smear were done in 300 patients attending the gynecology OPD. After obtaining informed consent both procedures were done in the same patients in the same visit. First conventional pap smear is taken which is followed by liquid based cytology. The study was conducted in 300 patients. Majority of the patients belonged to 31 to 35 years of age. Most cases belong to class II (upper middle class) according to modified Prasad classification. There is a higher percentage of detection of cases of Low grade squamous intra epithelial neoplasia in liquid based cytology when compared to conventional pap smear. (6.3% to 14%). There is an increased percentage of detection of Cases of High grade squamous intraepithelial lesion from 7.3% to 8.3% in liquid based cytology when compared to pap smear. The satisfactory smears interpreted by the pathologists on Liquid based cytology were 92.3% as compared to 15.7% on conventional papsmear. Commonly detected organisms were bacterial vaginosis and candida. The time taken by the pathologist to interpret LBC and conventional pap smear are 3secs and 5secs. The sensitivity of Liquid based cytology and conventional papsmear are 96.7% and 99.2%. The specificity of liquid based cytology and conventional papsmear are 83.9% and 98.8%. Liquid based cytology is strongly advocated in the best interest of public health. Liquid based cytology improves the quality of the sample and reduces the likelihood of false negative cytology results. Thus it will significantly improve early detection and treatment of cervical lesions.

Keywords: Papsmear, cytology, cervical cancer.

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INTRODUCTION

Cervical cytology was introduced by George Papanicolaou into clinical practice in 1940. In 1945, the Papanicolaou smear received the endorsement of the American cancer society as an effective method for the prevention of cervical cancer. Center of cytology in Vancouver, British Columbia published data which confirmed that cytologic screening leads to a reduction in the rate of invasive cancer of the uterine cervix. Several limitations of conventional pap smear were identified including inadequate transfer of cells to slide, in homogenous distribution of abnormal cells, presence of obscuring blood, inflammation or thick areas of overlapping epithelial cells. Liquid based cytology, thin layer technology was developed to address the limitation of Pap smear. More than 5,00,000 subjects have been studied with a preponderance of data indicating a significant benefit of liquid-based cytology, thin layer technology in the detection of cervical cancer precursor lesions and in the improvement of specimen adequacy. The present study was undertaken to evaluate the liquid based cytology technique and to compare the sensitivity and specificity of Liquid based cytology with conventional Papsmear.

MATERIALS AND METHODS

This comparative study was conducted on 300 patients attending the inpatient and outpatient department of gynecology in Shri balaji medical college and hospital from January 2020- January 2021. Patients will be from age group of 21 to 65 yrs.

Exclusion Criteria

- Bleeding per vaginum during the visit
- Pregnant women
- Uncooperative patients
- Treated cervical cancer cases

Procedure for conducting the study

In this study both liquid based cytology and conventional pap smear were done in 300 patients attending the gynecology OPD. After obtaining informed consent both procedures were done in the same patients in the same visit. First conventional pap smear is taken which is followed by liquid based cytology.

Conventional Pap Smear

Patient is asked to empty her bladder. Patient is made comfortable in lithotomy position. Sims speculum inserted and the cervix is visualized.

Papsmear is taken from the squamo columnar junction of the cervix using ayres spatula. The sample is spread on a glass slide and fixed immediately with cytological fixative. The obtained sample is sent for cytological examination.

LIQUID BASED CYTOLOGY

SAMPLE COLLECTION PROCEDURE-GYNECOLOGICAL PART

Cervical Sample Collection

Insert the cervix brush into the endocervical canal deep enough to allow the shorter bristles to fully contact the ectocervix. Then push gently and rotate the broom clockwise for 5 times.

Bristle Detachment

After collecting the sample detach the bristle into the vial with the lid and seal it firmly.

Collection Vial Sealing

After dropping the bristle into the vial, close the lid and seal it firmly.

Record And Transport

Fill the patient details over the vial and transport to lab for further processing.

SAMPLE PROCESSING PROCEDURE-LABAROTARY PART

Agitate the vial to obtain a homogenous transfer of sample. Transfer 5-6ml of the solution to a centrifuge tube prefilled with 4-5ml separator solution. Centrifuge the tube for 5 mins at 2000-3000rpm. Discard the supernatant and dilute the pellet with few drops of saline and dissolve it well. Transfer 50ml of the well dissolved sample using a micropipette onto a clean slide and smear over it using the tip. Stain the smear after drying it.

RESULTS

This study was done in 300 women.

Table 1: Age Distribution

Age groups	Frequency (n=300)	Percentage(%)
21-25 years	33	11.0%
26-30 years	53	17.7%
31-35 years	69	23.0%
36-40 years	47	15.7%
41-45 years	34	11.3%
46-50 years	28	9.3%
51-55 years	22	7.3%
56-60 years	09	3.0%
>60-65 years	05	1.7%
Total	300	100%
Age (Mean±SD)	38.4±12.7	

The age of the patients in this study ranged from 21-65 years. 23% of the patients were from age group 31-35 years. Youngest women of the study was of 21 yrs and oldest was 65years. The lowest incidence in the age group was 1.7% which ranged from 61-65 years

Table 2 : Socio-economic status

Socio-economic Class	Frequency (n=300)	Percentage %
Class I Upper class	73	24.3%
Class II Uppermiddle class	114	38.0%
Class III Middle class	63	21.0%
Class IV Lower middle class	36	12.0%
Class V Lower class	14	4.7%
Total	300	100%

The socioeconomic status was based on modified Prasad classification in this study.38% belonged to class II followed by 24.3% belonged to class I.4.7% belonged to class v.

Table 3: Clinical Presentation

Clinical presentation	Frequency (n=300)	Percentage %
White discharge PV	102	34.0%
Pain abdomen	63	21.0%
History of menorrhagia	83	27.7%
Irregular cycles	52	17.3%
Total	300	100%

Majority of the patients in this study 34% presented with white discharge per vaginum followed by menorrhagia which is 27.7%.17.3% presented with irregular cycles.

Table 4: Comparison Of Pathological Characteristics Of Liquid Based Cytology And Conventional Papsmear

Variables	CONVENTIONAL PAPSMEAR (n=300)			LIQUID BASED CYTOLOGY(n=300)	
	Frequency	Percentage	Frequency	Percentage	
Satisfactory					
Yes	47	15.7%	277	92.3%	
No	253	84.3%	23	7.7%	
Background					
Clean	205	68.3%	298	99.3%	
Others	95	31.7%	02	0.7%	
Overlapping					
No overlapping	0	0.0%	295	98.3%	
1+	8	2.7%	5	1.7%	
2+	214	71.3%	0	0	
3+	78	26.0%	0	0	

Depending upon the nuclear and cytoplasmic quality of cells, liquid based cytology had more number of satisfactory cases 260 (92.3%),more number of cases with clean background 281 (99.3%) and less overlapping of cells

Table 5: Incidental Detection Of Vaginal Infectious Agents In Liquid Based Cytology And Conventional Papsmear

Organisms	CONVENTIONAL PAPSMEAR n=24	LIQUID BASED CYTOLOGY n=45
Bacterial vaginosis (BV)	11	24
Trichomonas vaginalis (TV)	1	2
BV and TV	2	8
Actinimycosis	2	2
Candida	8	9
Total	24	45

In Liquid based cytology 45 smears were found to have infectious organisms, whereas in conventional pap smear only 24 smears were found to have infectious organisms.24 patients had infection with Bacterial vaginosis in liquid based cytology where as 11 patients in conventional papsmear.

These patients were treated with oral Antibiotics. Patients with bacterial vaginosis were treated with T.Metronidazole 500mg twice daily for 7 days. The cure rate was 75-84%.

Table 6: Time Taken By The Pathologist To Interpret Liquid Based Cytology And Conventional Papsmear

Mean time taken	Mean±SD
In Conventional pap smear	5.1±2.1 sec
In Liquid based cytology	3.03±1.4 sec

The time taken by the pathologist to interpret liquid based cytology is 3secs and for conventional papsmear is 5 secs. The difference in time taken is because of the quality of sample which is good in liquid based cytology.

Table 7: Results Of Liquid Based Cytology And Conventional Papsmear

Findings	LIQUID BASED CYTOLOGY (n=300)			CONVENTIONAL PAPSMEAR (n=300)
	Numbers	Percentage	Numbers	Percentage
Normal	155	51.7%	205	68.3%
Atrophic	24	8.0%	21	7.0%
ASCUS	45	15.0%	24	8.0%
LSIL	42	14.0%	19	6.3%
HSIL	25	8.3%	22	7.3%
Carcinoma	09	3.0%	09	3.1%
Total	300	100%	300	100%

Both liquid based cytology and conventional pap smear were done in 300 women in the same visit. The percentage of normal smears in conventional papsmear (68.3%) is more when compared to liquid based cytology (51.7%).The Atrophic smears were more in liquid based cytology (8%) when compared to conventional pap smear (7%).Smears with ASCUS is more in liquid based cytology (15%) when compared to conventional papsmear (8%).Liquid based cytology diagnosed more number of cases with low grade squamous intra epithelial lesion (14%) than conventional papsmear which is 6.3%.High grade squamous intraepithelial lesion smears were 8.3% in liquid based cytology when compared to conventional papsmear 7.3%.Both liquid based cytology and conventional papsmear detected equal percentage of cases with carcinoma (3%).

42 patients with low grade squamous intraepithelial lesion in liquid based cytology and 19 patients with low grade sqamous intraepithelial lesion in conventional papsmear were followed up with repeat papsmear after one year. Histopathological examination was done in patients with high grade squamous intraepithelial lesion and carcinoma in both liquid based cytology and conventional papsmear.

Table 8: Co-Relation Of Histopathology In Hsil And Carcinoma By Liquid Based Cytology And Conventional Papsmear

HISTOPATHOLOGICAL FINDINGS	Liquid based cytology		Conventional Papsmear	
	Numbers	Percentage	Numbers	Percentage
CIN 1	-	-	-	-
CIN 2	14	43.8%	13	44.8%
CIN 3	11	34.4%	8	27.6%
Carcinoma	6	18.8%	5	17.2%

Histopathological examination was done in patients who were diagnosed to have high grade squamous intraepithelial lesion and carcinoma in both liquid based cytology and conventional papsmear. In liquid based cytology 25 patients (8.3%) were diagnosed with high grade Squamous intraepithelial lesion and 9 patients (3%) with carcinoma. In conventional papsmear 22 patients were diagnosed with high grade squamous intraepithelial lesion (7.3%) and 9 patients (3%) with carcinoma. 34 patients with high grade squamous intraepithelial lesion and carcinoma in liquid based cytology where as 31 patients in conventional papsmear underwent histopathological examination.

34 patients in liquid based cytology were confirmed with the following histopathological findings:

- CIN 2- 14 patients (43.8%)
- CIN 3- 11 patients (34.4%)
- Carcinoma – 6 patients (18.8%)

31 patients in conventional papsmear were diagnosed with the following findings:

- CIN 2- 13 patients (44.8%)
- CIN 3- 8 patients (27.6%)
- Carcinoma- 5 patients (17.2%)

Table 9: Statistical Significance

Case distribution in Liquid based cytology n=300			Case distribution in Conventional papsmear n=300			
Category	No. of cases	Percentage	Category	No. of cases	Percentage	p value
LSIL	42	14.0%	LSIL	19	6.3%	0.0470 S
HSIL	25	8.3%	HSIL	22	7.3%	0.145

P value in this study is significant for Low grade squamous intraepithelial lesion.

Table 10: Liquid Based Cytology

Test results	Disease present	Disease absent	Total
LBC positive	30 TRUE POSITIVE	2 FALSE POSITIVE	32
LBC negative	1 FALSE NEGATIVE	248 TRUE NEGATIVE	249
Total	31	250	281

19 patients were lost to follow up in this study. In liquid based cytology the total number of true positives were 30. False positive cases were 2. False negative and true negative cases in liquid based cytology were 1 and 248 respectively.

Table 11: Conventional Pap Smear

Test results	Disease present	Disease absent	Total
CPS positive	26 true positive	3 false positive	29
CPS negative	5 false negative	247 true negative	252
Total	31	250	281

The number of true positive cases in conventional pap smear was 26. The false positive patients in liquid based cytology and conventional pap smear were 2 and 3 respectively. Hence conventional papsmear has picked up one more false positive True negative cases in liquid based cytology and conventional pap smear were 248 and 247 respectively. Hence almost equal number of healthy patients are correctly identified as healthy. The most important is false negative patients. In liquid based cytology there was one false negative patient and in conventional papsmear there were 5 false negative patients. Pap smear has diagnosed 5 positive smears as normal.

This proves that liquid based cytology reduces the likelihood of false negative cytology results than liquid based cytology.

Table 12: Sensitivity And Specificity

Variable	LIQUID BASED CYTOLOGY	CONVENTIONAL PAPSMEAR
Sensitivity	96.7%	83.9%
Specificity	99.2%	98.8%

The sensitivity and specificity of liquid based cytology was 96.7% and 99.2% whereas conventional pap smear was 83.9% and 98.8% respectively.

DISCUSSION

Papsmear is one of the best available screening methods for early detection of cervical precancerous lesions. Despite being credited with a 70% reduction in the mortality for cervical cancer, the false negative rate is still a cause of concern. Two third of the overall false negative rate can be attributed to sampling errors.

Liquid based cytology has been developed to address the sampling problems of conventional pap smear In this study the mean age of the study participants was 38.4±12.7 years. Majority of them belonged to 31 to 35 years followed by 26 to 30 years and only few patients were in age more than 60 years. This finding was compared to that reported by Richart et al.

In our study out of 300 patients, 114 patients (38%) belonged to class II. This finding was similar to that noted by christopherson and Parker.

The most common presenting complaint in our study was white discharge per vaginum.

In our study the detection of Low grade squamous intra epithelial lesion increased from 6.3% to 14% with Liquid based cytology than with Conventional pap smear and High grade squamous intra epithelial lesion increased from 7.3% to 8.3% with Liquid based cytology than Conventional pap smear.

Hutchinson et al showed that fewer than 20% cells collected by Conventional pap smear were transferred on to slide and thus explained the high prevalence of false negative rate. Diaz and kabawat reported increased detection of pre-malignant precursors on Liquid based cytology when compared to Conventional pap smear. The percentage of cases with Low grade squamous intraepithelial lesion varies from 0.6 to 2.7% and of High grade squamous intraepithelial lesion from 0.3 to 0.5%.The findings in this study was compared with the study of sherwani et al.

In our study the satisfactory smears on Liquid based cytology were 92.3% as compared to 15.7% on Conventional pap smear. Similarlyweintraube and Morabia have reported increased number of satisfactory cases (72.2% to 92%) on Liquid based cytology than Conventional papsmear. All drying artefact and cytolysis is almost absent or minimal with Liquid based cytology because of immersion of cells into the liquid fixative and specimen adequacy was greatly improved due to absence of blood, mucus and inflammatory cells. Only conventional smears were unsatisfactory due to thick smears which was not a problem with Liquid based cytology due to even distribution of cells.

The microscopic details of infectious agents were enhanced in Liquid based cytology with Bacterial vaginosis (24cases) followed by candida (9cases) followed by trichomonas vaginitis (8 cases).This study was compared with the study of vikranth et al.

In our study the sensitivity and specificity of Liquid based cytology was 96.7% and 99.2% and of Conventional pap smear was 83.9% and 98.8% respectively. Boliock et al reported that the sensitivity and specificity of liquid based cytology was 95.2% and 58% respectively where as on Conventional pap smear it was 85% and 36% respectively. This study result is compared with boliock et al.

SUMMARY

- The study was conducted in 300 patients.
- Majority of the patients belonged to 31 to 35 years of age.
- Most cases belong to class II (upper middle class) according to modified Prasad classification.
- There is a higher percentage of detection of cases of Low grade squamous intra epithelial neoplasia in liquid based cytology when compared to conventional pap smear.(6.3% to 14%). P value in this study was significant for LSIL.
- There is an increased percentage of detection of Cases of High grade squamous intraepithelial lesion from 7.3% to 8.3% in liquid based cytology when compared to pap smear.
- The satisfactory smears interpreted by the pathologists on Liquid based cytology were 92.3% as compared to 15.7% on conventional pap smear.
- Commonly detected organisms were bacterial vaginosis and candida.
- The time taken by the pathologist to interpret LBC and conventional pap smear are 3secs and 5secs.
- The sensitivity of Liquid based cytology and conventional papsmear are 96.7% and 99.2%.
- The specificity of liquid based cytology and conventional papsmear are 83.9% and 98.8%.

CONCLUSION

Liquid based cytology is strongly advocated in the best interest of public health. Liquid based cytology improves the quality of the sample and reduces the likelihood of false negative cytology results. Thus it will significantly improve early detection and treatment of cervical lesions.

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