ORIGINAL RESEARCH PAPER

Gynaecology

TO STUDY LIQUID BASED CYTOLOGY AS A SCREENING TOOL FOR ABNORMAL CERVICAL CYTOLOGY

KEY WORDS: Liquid base cytology, Cervical biopsy

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ABSTRACT

Aim – To determine sensitivity and specificity of liquid base cytology for detection of abnormal cervical cytology **Methodology-** diagnostic evaluation study Sample size- 370 **Result –** Sensitivity – 96.9% Specificity – 91.7% Conclusion – LBC has high diagnostic accuracy in detecting abnormal cervical cytology compared to pap smear

INTRODUCTION

Cervical cancer is the second highest cause of cancer related mortality in women (1, 2, 3, and 4). Morethan80% of new cervical cancer cases occur in developing and under developed countries.The progression of this cancer is slow with pre-cancerous period of 10-20 years. The Indian Council of Medical Research (ICMR) says the incidence of cervical carcinoma in India varies from 20 to 35 /100,000 women between age group 35 to 64 years in comparison with developed countries(1 to 8 /100,000)women(1).Although routine cytological screening has resulted in large reduction in the cervical cancer burden in our country, still the incidence rates continued to be high for want of effective screening programs.

Pap smear was the initial screening method for detection of abnormal cervical cytology. The sensitivity of this screening method is 60to 80%. It is also associated with significant number of false negative cases. Liquid Based Cytology wasintroduced to overcome the shortcomings of Pap smear method(1).LBC has more representative transfer of cells from collection device to glass slide, reduction in number of unsatisfactory cytology samples and increased detection of abnormal cytology compared to pap smear screening (2).

This study is conducted to find out the sensitivity and specificity of Liquid Based Cytology as a screening tool for abnormal cervical cytology

OBJECTIVES

1.To determine the sensitivity of the Liquid Based Cytology
2.To determine the specificity of the Liquid Based Cytology

METHODOLOGY

This diagnostic evaluation study was conducted at the Department of Obstetrics and Gynecology in a tertiary care hospital. The study included randomly selected women attending gynecology OPD and who fulfilled the inclusion criteria. Women were counseled regarding the procedure and informed consent obtained. The social, medical, obstetric and gynaecological history was obtained and a general and pelvic examination was performed with the patient in lithotomy position and under good illumination. An un-lubricated Cusco's self-retaining speculum was introduced into vagina to visualize the cervix. The samples are collected from cervix usingendocervical broom issued by the manufacturer, which was inserted into the endo-cervical canal and rotated 360 degrees.

Then, the brush is detached and placed into a vial containing fixative issued by the manufacturer for transport. The vial container is then shaken and then transported. Cytological smear processed and analyzed using manual method. Bethesda system of reporting of cervical smear has used for reporting of the smears. The gold standard used was cervical tissue biopsy in case of abnormal smear.

Reporting system: Results of the cytology examination were reported using the classification of Bethesda System The statistical data collected in excel format was coded for various parameters and analysis was carried out using SPSS version 20.

RESULTS

Out of 370 cases studied the following results were obtained.

Table: 1) Distribution of findings on LBC among the cases studied.

LBC Findings	No. of cases	% of cases
NILM(Expanded form off all)	267	72.2
HSIL	26	7.0
ASC-US	25	6.8
Inflammatory	18	4.9
LSIL	17	4.6
Malignant	7	1.9
ASC-H	5	1.4
Inadequate	3	0.8
Atrophic	2	0.5
Total	**370**	**100.0**

Of 370 cases studied, 267 (72.2%) had NILM, 26 (7.0%) had HSIL, 25 (6.8%) had ASC-US, 18 (4.9%) had inflammatory, 17 (4.6%) had LSIL, 7 (1.9%) had malignant, 5 (1.4%) had ASC-H, 3 (0.8%) had inadequate and 2 (0.5%) had atrophic findings on LBC.

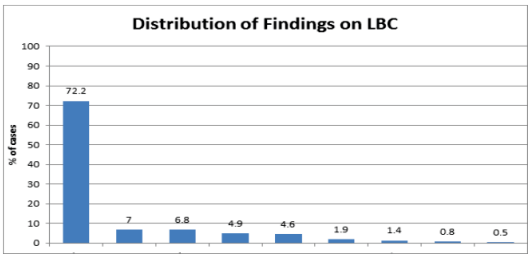


Figure:1 Distribution of findings on LBC among the cases studied.

Table: 2 Distribution of overall findings on LBC among the cases studied.

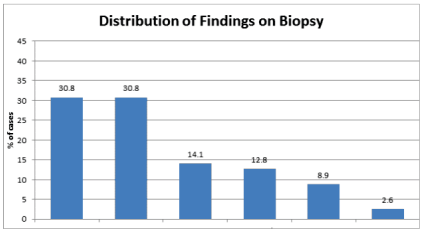
LBC Findings	No. of cases	% of cases
Negative	294	79.5
Positive	76	20.5
Total	**370**	**100.0**

Of 370 cases studied, 294 (79.5%) had negative findings and 76 (20.5%) had positive findings on LBC.

Table:3 Distribution of findings on biopsy among the cases studied.

Biopsy Findings	No. of cases	% of cases
CIN1	24	30.8
CIN2	24	30.8
Squamous carcinoma	11	14.1
Normal	10	12.8
CIN3	7	8.9
Cervicitis	2	2.6
Total	**78**	**100.0**

Of 78 cases on whom biopsy was done, 24 (30.8%) had CIN1, 24 (30.8%) had CIN2, 11 (14.1%) had squamous carcinoma, 10 (12.8%) had normal biopsy finding, 7 (8.9%) had CIN3 and 2 (2.6%) had cervicitis.



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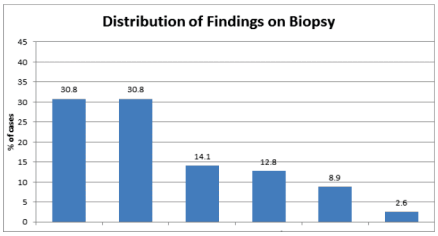

Figure: 2 Distribution of findings on Biopsy among the cases studied.

Table: 3Distribution of overall findings on biopsy among the cases studied.

Biopsy Findings	No. of cases	% of cases
Negative	10	12.8
Positive	68	87.2
Total	**78**	**100.0**

Of 78 cases on whom biopsy was done, 10 (12.8%) had negative findings and 68 (87.2%) had positive findings on biopsy.

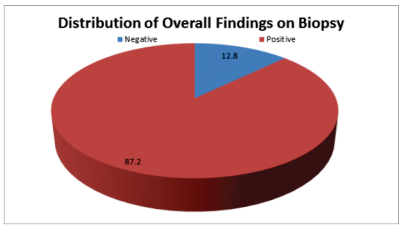

Figure:3 Distribution of overall findings on Biopsy among the cases studied.

Table: 4 Distribution of diagnosis by LBC and by Biopsy as a Gold standard.

	Diagnosis by Biopsy						
	Positive		Negative		Total		Kappa-value (P-value)
Diagnosis by LBC	n	%	n	%	n	%	
Positive	64[TP]	97.0	1[FP]	8.3	65	83.3	0.857 (0.001***)
Negative	2[FN]	3.0	11[TN]	91.7	13	16.7	
P-value	**66**	**100.0**	**12**	**100.0**	**78**	**100.0**	

P-value by Chi-Square test (Fisher's exact probability test).
P-value<0.05 is considered to be statistically significant.
***P-value<0.001.
TP – True positive, FN – False negative, FP – False positive, TN – True negative

Of 66 positive cases by Biopsy, 64 (97.0%) were positive by LBC and 2 (3.0%) were negative by LBC. Of 12 negative cases by Biopsy, 1 (8.3%) was positive by LBC and 11 (91.7%) were negative by LBC.

Distribution of diagnosis by LBC is significantly associated with the diagnosis by Biopsy among the cases studied with relatively higher Cohen-Kappa value =0.857 (P-value<0.001). Higher Co-hen Kappa value indicates that there is relatively higher agreement between diagnosis by LBC and diagnosis by Biopsy.

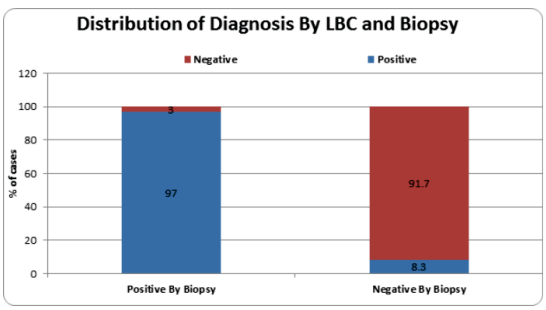

Figure:4 Distribution of diagnosis by LBC and by Biopsy as a Gold standard.

Table: 5 Distribution of diagnostic efficacy indices of LBC against Biopsy as a Gold standard.

Diagnostic Efficacy indices of LBC	Value (%)
Sensitivity	96.9
Specificity	91.7
Positive predictive value (PPV)	98.5
Negative predictive value (NPV)	84.6
Accuracy	96.1

The distribution of diagnostic efficacy indices such as sensitivity, specificity, Positive predictive value (PPV), Negative predictive value (NPV) and accuracy of LBC against Biopsy findings as a Gold standard is 96.9%, 91.7%, 98.5%, 84.6% and 96.1% respectively.

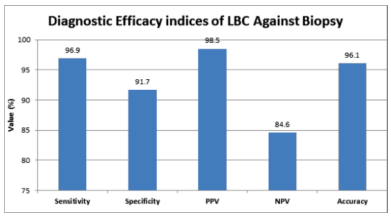

Figure:5Distribution of diagnostic efficacy indices of LBC against Biopsy as a Gold standard.

DISCUSSION

Cervical cancer is the second highest cause of cancer related mortality in women (1). Among South Asian Countries India accounts for the maximum number of cancer cervix. Most cervical carcinomas occur in women who have never been screened or who have not been screened adequately.

This study was carried out with the aim of finding the sensitivity and specificity of liquid based cytology. A total of 370 women between the ages of 21-75 years are included in this study.

The outcome of the study are analysed with respect to various factors which are as follows,

As per this study Liquid based cytology as a screening tool for abnormal cervical cytology the following observations obtained

1.Sensitivity - 96.9%
2.Specificity - 91.7%
3.Positive predictive value - 98.5%
4.Negative predictive value - 84.6 %
5.Accuracy - 96.1%

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Study conducted by Shanmugapriya et al, the differences of sensitivity and specificity between LBC, PAP smear and colposcopy in detection of premalignant lesions were analysed using the chi square test. The sensitivity of LBC (89.5%) was significantly higher than sensitivity of PAP smear (47.37%). P<0.001.The specificity of PAP smear (95.06%) was higher than LBC(77.16%). The statistical analysis between LBC and PAP smear; LBC and colposcopy were significant (P=0.000<0.05) (1).

Study conducted by Park etal In a population with cervical abnormalities, LBC is more specific than and as effective as conventional smear in detecting cervical epithelial cell abnormalities. A study conducted by Ovadia Abulafia et al Anoverall sensitivity of 76% for Thin Prep-prepared cervicalslides versus 68% for conventionally prepared smear and specificity of 86% for Thin Prep-prepared cervical slides versus 79% for conventionally prepared Papanicolaou smears.

A study done by Albertus et al the test positivity rates of liquid-based cytology are similar to conventional cytology .They found a strong reduction in unsatisfactory rates in the experimental liquid-based arm as compared with conventional cytology (OR 0.29, 95% confidence interval 0.23–0.38)(70).Study conducted by Chinkaetal the sensitivity and specificity of LBC was 100% and 100% respectively and conventional Pap smear 86% and 97% respectively

Table:6 Sensitivity and Specificity

Studies	Sensitivity	Specificity
This Study	96.9	91.2
Beerman et al	96.2	98.2
Chinaka et al	100	100
Shanmughapriya et al	89.5	77.16
Albertus et al	100	86

CONCLUSION

Globally, cervical cancer continues to be one of the most common cancers among females In 2012, it was estimated that there were approximately 527 600 new cases of cervical cancer with 265 700 deaths annually. The majority of new cases and occur in low-resource regions or among people from socioeconomically weaker sections of society My study is focussed on finding out the sensitivity and specificity of the Liquid Based Cytology. Liquid based cytology was found to have high diagnostic accuracy compared to conventional cytology in this research work. The study confirms previous reports of decreased numbers of unsatisfactory samples, increased satisfactory samples, and increase detection of LSIL, HSIL, Carcinoma and true positive result with liquid based cytology. it improves the quality of samples andreduces the likelihood of false negative result, thereby significantly improves early detection and treatment of pre malignant cervicallesions.

Strengths of study

1 Diagnostic Evaluation Study
2. High follow up
3. Almost all our patients had similar socio economic status and education

Limitations of the study

1. Single Centre study
2. Small Sample size
3. We cannot exclude the possibility of other cofounding from un measured co variants

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Conflict of interest Authors declare none.

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