Comparison between Thin Prep® Preparation (Liquid Based Cytology) and Conventional Pap Smears of Cervical Smear Cytology Lesions – A Study from Kanyakumari, Tamilnadu, India

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ABSTRACT

BACKGROUND

The major cause of mortality among women is cancer of the uterine cervix. It is the second most common cancer worldwide. Pap smear is done as a method of cervical screening to detect precancerous and cancerous lesions of the cervix. Early detection of these lesions prevent the number of deaths from cervical cancer. Liquid based cervical cytology was developed to improve the diagnostic accuracy of pap smears. The main purpose of this study was to compare the profile of distribution of cervical smear cytology lesions obtained by thin prep preparation (liquid based cytology) and conventional pap method among women in the age group of 25 – 60 yrs.

METHODS

This is a cross sectional study done among 110 women from the outpatient department of Obstetrics and Gynaecology. Conventional and liquid based cytology smears were taken simultaneously from the same women and reported according to the 2001 Bethesda system.

RESULTS

Majority of the women included in this study fall in the age group of 41 - 50 years [65 (59.1 %)]. Women with a history of persistent vaginal infection were 13 (11.8 %). Out of the 110 pap smears taken by both conventional and liquid based methods, unsatisfactory smears were not detected in liquid based cytology and 6 (5.5 %) unsatisfactory smears were found in conventional pap method. In liquid based cytology, inflammatory smears were detected more (80 %), atrophic smears (2.7 %), smears with features of atypical squamous cells of undetermined significance (ASCUS) were 4.5 %, low-grade squamous intraepithelial lesion (LSIL) were 3.6 %, and smears with high-grade squamous intraepithelial lesion (HSIL) were 0.9 %. Epithelial cell abnormalities were found to be high in liquid based cytology.

CONCLUSIONS

Abnormal epithelial lesions were detected more in liquid based cytology (thin prep method). The number of unsatisfactory smears were found to be decreased when compared to conventional pap method.

KEY WORDS

Bethesda Cervical Cytology, Cervical intraepithelial lesion, Conventional Pap Smear, Liquid Based Cytology Smear

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BACKGROUND

Cancer of the uterine cervix is the leading cause of mortality and morbidity among women throughout the world. India has got a high burden of cervical cancer and accounts for one fifth of the world burden of cervical cancer.¹ Most of the known associated risk factors of developing cervical cancer are multiple childbirths, early age at marriage, and multiple sexual partners, long term use of oral contraceptive pills, hormones, poor socioeconomic status, lack of education, tobacco smoking, genital infections with herpes and Human Papilloma Virus (HPV). Cervical cancer is caused by sexually acquired infection with certain types of HPV. Infection with the Human papilloma virus is highly transmitted through sexual contact and most of the women are infected with HPV shortly after the onset of sexual activity. Among the many forms of HPV, HPV 16 and 18 are strongly associated with cervical cancer.² Prolonged HPV infection is essential for the progression of precursor lesions which develops into cervical cancer. HPV DNA integrates into host genome which is necessary for the development of cervical cancer. This leads to splitting of the E2 gene. They induce enhanced expression of HPV derived viral oncoproteins (E6 and E7). E6 binds and degrades p53 and E7 binds and degrades Retinoblastoma (Rb) tumor suppressor protein. This results in uncontrolled cellular proliferation due to release of E2F transcription factor. This leads to increase in p16 protein expression - a predictive biomarker for the identification of cervical intra epithelial lesion.³

Cervical cancer is commonly found in the age group of women between 30 – 59 years and the peak age of incidence may vary among the populations.⁴ Most of the lesions were identified in the advanced stages due to lack of knowledge. However the incidence has been brought down by doing regular cervical cytology screening. So early detection of precursor lesions in the cervix can be detected by cytological screening by doing a pap smear. It is a simple, safe and non invasive method and is a widely accepted screening technique.⁵

According to American College of Obstetrics and Gynecology effective cervical cancer prevention is to identify the precursor lesions and to provide appropriate treatment to women. Precursor lesions will progress to invasive cervical cancer if left untreated.⁶

In conventional Pap smear the sensitivity is detected to less than 50 % due to inadequate sampling technique and slide preparation by obscuring elements like mucus, blood, inflammatory cells and in homogenous distribution of epithelial cells. Liquid Based Cytology (LBC) was developed as a replacement technique to overcome the drawbacks that were obtained in conventional Pap smears. Liquid based cytology simplifies collection method, improves fixation and reduces the unsatisfactory smears. HPV DNA testing is also performed with the remaining sample.⁷

Human papillomavirus vaccines prevent human papilloma virus infection. Newer vaccines have been approved for the prevention of cervical cancer. Cervarix[®] (GlaxoSmithKline) and Gardasil[™] (Merck and Co) vaccines prevent infection with HPV types 16 and 18.⁸ Vaccination is the most cost effective public health measure against cervical cancer. However cervical screening cannot be replaced by vaccination. Therefore screening programmes may still need to be strengthened.

Since early detection predicts better prognosis, one of the most effective way of preventing cervical cancer is regular cytological screening and early diagnosis.⁹ Pap smear has been commonly applied as a screening method for huge population.¹⁰

The present study was undertaken to describe the profile of distribution of cervical smear cytology lesions among women and comparison was done between conventional and thin prep method.

METHODS

It was a cross sectional study on cervical exfoliative cytology smears and was conducted at the Department of Pathology in collaboration with the Outpatient department of Obstetrics and Gynaecology in Sree Mookambika institute of Medical Sciences, Kulasekharam, kanyakumari, Tamilnadu. This study was undertaken from April 2013 to March 2014 after obtaining approval from the Institutional Ethical Committee. Informed consent was obtained from all the women included in the study. Women were selected in the age group of 25 - 60 years with symptoms of foul smelling leucorrhea, abnormal vaginal discharge, postcoital bleeding, abnormal uterine bleeding, bleeding after menopause and / or any other abnormal findings on speculum examination. Unmarried women, pregnant women, women with post - hysterectomy or post - chemotherapy / radiotherapy were excluded from the study. By convenient sampling, the sample size was selected to be 110. Results were generalizable to similar populations.

The recruited patients were advised to avoid vaginal medications, contraceptives or douches for 2 days before doing a pap smear. They were also asked to avoid sexual intercourse for the night before the appointment. Smears were taken 2 weeks after the first day of the last menstrual period.

After inspection of the cervix, the Ayres spatula was inserted into the cervical canal, rotated at 360 degrees and the material was scrapped from the squamo-columnar junction and then spread on to labeled glass slides. The smears were fixed with 80 % isopropyl alcohol and sent to the cytopathology laboratory where they are stained by Papanicolaou method. Simultaneously, for liquid based cytology (Thin Prep method), cervix brush was used. Each brush with the material was rinsed in a vial containing Preserv Cyt solution.

The Thin Prep sample vial was then capped, labelled and sent to the laboratory. The vial was then processed in a Thin Prep Processor and the slides obtained were then stained by pap stain. Reporting of the cervical pap smears was based on the Bethesda system 2001 method.

Statistical Analysis

The data was entered in to Microsoft Excel and scrutinized using the SPSS version 20. The socio-demographic details of the study population were described using descriptive statistics such as frequencies. Fisher's exact test and chi square was used to identify the difference pattern (lesions) between two smears.

RESULTS

Among the 110 women participated in the study, majority (65, 59.1 %) were in the age group of 41 to 50 years, 28 (25.5 %) were in the age group of 31 – 40 years, 13 (11.8 %) were between 51 – 60 years and 4 (3.6 %) women were aged between 25 – 30 years. Most of the women in this study had earned education up to the high school or above (N = 82, 74.6 %). 34 (30.9 %) women were employed while the rest were homemakers.

Method	Unsatisfactory to Normal	Inflammatory and Atrophic	Abnormal (Includes ASCUS, LSIL, HSIL)	Total	Chi ² value	P - Value
Conventional method	14	92	4	110	3.66	0.16
Liquid based cytology	9	91	10	110		
Total	23	183	14	220		

Table 1. Observation of Cervical Lesions in Liquid Based Cytology Compared with Conventional Pap Method

The number of unsatisfactory lesions by the conventional method was 6 while there were no unsatisfactory lesions in the Liquid Based Cytology method. However, the two methods did not significantly differ from each other in detecting various types of lesions.

Age Category	Normal and Inflammatory	Lesions Atrophic and Abnormal (Includes ASCUS, LSIL, HSIL)	Total	P - Value (Fisher's Exact Test)
Lower (<30 years)	28	4	32	1.0
Higher (>30 years)	69	9	78	
Total	97	13	110	

Table 2. Comparison of Lesions Identified by Liquid Based Cytology Based on Age Categories

80 % of the abnormal lesions (N = 8) and 71.6 % of inflammatory lesions (N = 63) were detected among those aged more than 30 years. However the lesions did not differ significantly between the two age groups.

Age at marriage Category	Normal and Inflammatory	Lesions Atrophic and Abnormal (Includes ASCUS, LSIL, HSIL)	Total	P - Value (Fisher's Exact Test)
Lower (<30 years)	35(85.3 %)	6(14.6 %)	41(100 %)	0.55
Higher (>30 years)	62(89.9 %)	7(10.1 %)	69(100 %)	
Total	97(88.2 %)	13(11.7 %)	110(100 %)	

Table 3. Comparison of Lesions Identified by Liquid Based Cytology Based on Age at Marriage

Inflammatory lesions were higher among both age groups (88, 80 %) as compared to other types of lesions. However, it was seen that the type of lesions did not vary significantly with the age at marriage.

Majority of the cervical lesions (80 %, N = 88) were of the inflammatory type. This was also the most common type of

lesion detected among both groups. However more abnormal epithelial lesions were detected among primipara mothers.

Deliveries	Normal	Inflammatory	Lesions Atrophic	Abnormal (Includes ASCUS, LSIL, HSIL)	Chi ² Value	P - Value
Primipara / second	6	63	3	8	1.62	0.65
Multipara	3	25	0	2		
Total	9	88	3	10		

Table 4. Distribution of Lesions by Number of Childbirths

Figure 1. Conventional Pap Smear and Liquid Based Cytology of Cervical Smear Showing ASCUS Lesion Conventional PAP-ASCUS(40X)

Figure 2. LBC - ASCUS (High Power View)

DISCUSSION

Cervical screening has become an essential screening test for the early detection of abnormal cervical lesions. Among the several screening methods, conventional pap smear is the most common and routine method which has been applied so far. It is a simple test which prevents the number of deaths due to cervical cancer. Liquid based cytology, a thin layer preparation was performed in this study to compare and determine the accuracy with conventional pap smears.

In this study the number of unsatisfactory smears were detected more in the conventional method. The reason for this was occurrence of thick smears, haemorrhage and inflammation. In liquid based cytology unsatisfactory smears were not made out. A similar statistically significant finding was seen in a study done by Chinaka CC et al.¹¹ who also found more unsatisfactory smears with conventional method than Liquid based cytology.

Women included in this study were in the age group of 25 - 60 yrs. Among the 110 women screened, many of them belong to the age group of 40 - 50 yrs. In LBC method, the epithelial

abnormalities - Atypical squamous cells of undetermined significance (ASCUS), Low-grade squamous intraepithelial lesion (LSIL), High-grade squamous intra epithelial lesion (HSIL) were detected high in women more than 30 years. These lesions were detected less in women in the age group less than 30 years. In a study conducted by Ranabhat et al.¹² it was seen that 80 % of abnormal epithelial lesions were found in the age group of above 40 years. Another study done by Misra et al.¹³ in our country found that 51.5 % of squamous intraepithelial lesion cases and 75.3 % of carcinoma cervix were detected in women above 40 years of age.

Our study also revealed that out of 110 cases, abnormal epithelial lesions were found in 10 cases (9.09 %) by thin prep method whereas conventional pap method detected abnormal lesions in only 4 cases (3.63 %). Thin prep identified more abnormal epithelial lesions in our study. A study conducted by Sherwani RK et al.¹⁴ also showed quite similar findings of cervical intraepithelial abnormal lesions of 42 cases (26.2 %) by pap smear method and 24 cases (15 %) in conventional method out of 160 women studied.

Mayavati Mhaskeet et al.¹⁵ in their study of risk factor association and cervical dysplasia studied the association between early age of marriage and cervical cancer. Women married earlier were more common in the age group of 18 - 26 years in our study. There was no much difference in the distribution of epithelial lesions found in both age groups. More or less the lesions were found to be similar in both age groups. Another study by Sreejatha Raychaudhuri et al.¹⁶ showed that early age of marriage (indicative of an early exposure to sexual activities) and early pregnancy were risk factors for carcinoma cervix.

In this study most of the women delivered between the ages of 18 to 26 years (90 %) and women who had two deliveries were found more 57 (51.8 %). High parity was not noticed. ASCUS, LSIL, HSIL were found to be detected more among women with two deliveries. A study done by Misra et al.¹³ showed the frequency of squamous intraepithelial lesions were more obvious and statistically significant between para 2 and 3. Our study showed the detection of smears which were negative for intraepithelial lesions were more or less equal in numbers (80 %) in both conventional and LBC. A similar result was noted in the study conducted by Annie N. Y. Chung et al.¹⁷

CONCLUSIONS

After interpretation of 110 cervical cytology smears, unsatisfactory smears were not found in liquid based cytology in our study. LBC was easier to screen because the sample were liquid based and detected more abnormal epithelial lesions with sample being more representative. There was no statistically significant difference between LBC and conventional pap observed in our study. Although there have been a number of technical advances in cervical cancer screening, LBC showed a better performance as a screening test due to practical advantages but due to the high cost of LBC, conventional pap smear still remains the screening test of choice in hospitals.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

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