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Conventional Pap Smear and Liquid Based Cytology for Cervical Cancer Screening - A Comparative Study

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Abstract: ***Background: The Conventional pap smear has been utilized for cervical cancer screening for more than 50 years. Despite being credited with a 70% reduction in mortality for cervical cancer, the false negative rate is still a cause for concern. It is widely acknowledged that 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. The aim of the study was to compare conventional pap smear and Liquid based cytology for cervical cancer screening. Method: Prospective comparative study of 200 Women who are sexually active and reported to the OPD for gynecological consultation, in the age group of 21-65 years at MGM Women and Children's Hospital, Kalamboli Both conventional pap and liquid based cytology was performed on the same patient. Results: LBC was found to be a better alternative to conventional smear because of lower rate of unsatisfactory smears. Also, it has advantages of less obscuring by blood, mucus material and inflammatory cells. Conclusion: 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 lesions.***

Keywords: Conventional Pap smear, LBC, CA Cervix screening, HPV

1. Introduction

Cervical cancer is a common cancer among women worldwide[1]. In developing countries, it is the second most common cancer and third highest reason for death due to cancer after breast and lung cancer.Over 85 percent of new cases are diagnosed in resource-limited countries where it is the most common cancer in women after breast cancer[2]. "Cervical cancer can have devastating effects with a very high human, social, and economic cost, affecting women in their prime. But this disease should not be a death sentence, even in poor countries," explains Dr.Rengaswamy Sankaranarayanan, a lead investigator for an IARC research project with a focus on cervical cancer screening in rural India. Sexually transmitted human papillomavirus (HPV) infection is the most important risk factor for cervical intraepithelial neoplasia (CIN) and invasive cervical cancer. Worldwide, the prevalence (%) of HPV 16 and/or HPV 18 among women with normal cytology is 4.1%. HPV serotypes 16 and 18 account for nearly 76.7% of cervical cancer in India. Globally, high-risk types HPV 16 and 18 contribute to more than 70% of all cervical cancer cases[3]. In India, cervical cancer is the second leading cause of new cancer cases and cancerrelated deaths among gynaecological cancers in females, with an estimated 96,922 new cases and 60,078 deaths each years[3-18].

The available methods for screening are the Papanicolaou (pap) test (cytology) and Human Papilloma virus (HPV DNA) testing[19]. Screening can detect precursors and early-stage disease for both types of cervical cancer including squamous cell carcinoma and adenocarcinoma. Treatment for precursor lesions will prevent the development of invasive cervical cancer and thereby reduce cervical cancer related morbidity and mortality.In India, women do not have access to effective screening program and without major improvement in cytology services it will not be possible to screen even 25 percent of the population once in a lifetime in near future[20]. One study reported that only 63.0% of women in developing countries received cervical cancer screening[21]. Evidence for using colposcopy in the absence of a squamous intraepithelial lesion by the conventional cytology is fast gaining important position in cervical cancer screening.[22].

Park et al[24] established that the sensitivity of the conventional pap smears for the detection of cervical cancer precursors was less than 50%. Several limitations of conventional smear were identified including inadequate transfer of cells to slide[25], in homogenous distribution of abnormal cells, presence of obscuring blood, inflammation or thick areas of overlapping epithelial cells[26]. Liquid based; thin layer technology was developed to address the limitation of Conventional pap smear. Some advantages of LBC are the presence of 100% of the collected sample a fixative liquid with the possibility to perform cytochemical tests, molecular biology test and 3 new exams,if required, using the same sample. Besides, there are less false-negative results and unsatisfactory smears. Also, cell preservation with a sample of higher quality enables a better interpretation[27], and reduces the length of exams in 30%, therefore increasing the productivity of laboratories[28]In view of the emerging need of finding an effective tool for detecting recurrence of cervical cancer, this study was planned to assess the efficacy of LBC as a method for cytological follow up and detection of cancer cervix and compared with Conventional pap smear method to find the best screening method for detection of cancer in such patients.

2. Materials and Methods

Prospective comparative study of 200 Women who are sexually active and reported to the OPD for gynecological consultation, in the age group of 21-65 years at MGM Women and Children's Hospital Kalamboli, both conventional pap and liquid based cytology was performed in the same patient at the same sitting

Inclusion Criteria:

1) Women who are sexually active and reported to the OPD for gynecological consultation.
2) Women in the age group of 21-65 years.
3) Patients willing and give consent for the procedure.

Exclusion Criteria:

1) Age < 21 and > 65 Years
2) Antenatal and Postnatal mothers (Puerperium Period)
3) Previous screening test taken
4) Proven preinvasive lesions & on treatment
5) Menstruating women/Active vaginal Bleeding
6) Pervious surgery on cervix
7) Cases of HIV/STD
8) Utero cervical prolapse

Study Methodology

A detailed history of the patient was taken and the patient was informed about the screening procedure, Informed consent was taken, Clinical data were collected from every woman, including age, menstrual status, any contraception method, and any symptoms (discharge, vaginal bleeding, pelvic pain, and others).Both conventional pap and liquid based cytology was performed in the same patient.

Conventional pap smear (CPS): The smears were taken by a gynecologist with patient in dorsal position under direct vision by using Cusco speculum. Sample taken using Cytobrush from the Squamo-columnar junction. Cytobrush was rotated against the ecto-cervix for a 360 degree rotation so as to include the transformation zone. Material from the Cytobrush was spread onto a clean glass slide and fixed by Bio spray (ethyl alcohol) for conventional method. They were then labelled, stained by the standard Papanicolaou method and studied by a pathologist.

Liquid Based Cytology (LBC): The Sure Path process begins with gynaecologist using a cervical brush (Cytobrush with detachable head- SurePath) Cytobrush was rotated against the ecto-cervix for a 360 degree rotation to collect the specimen. Rather than smearing cells collected by the sampling devices on a glass slide, the heads of the sampling devices detach from the handle and are placed into a vial of SurePath Preservative Fluid. The vial was capped, labeled, and sent with 32 appropriate paperwork to the laboratory for processing (papinoclou stain and study) The heads of the sampling devices are never removed from the preservative vial containing the collected sample

Ethical clearance:

The project was started after clearance certificate from the institutional ethics and scientific committee was obtained.

3. Results

The present prospective comparative study was conducted in the Department of Obstetrics and Gynecology MGM Women and Children Hospital, Kalamboli, Navi Mumbai among women who are sexually active and reported to the OPD for gynecological consultation. Both conventional pap and liquid based cytology was performed in the same patient. The aim of the study was to compare conventional pap smear and Liquid based cytology for cervical cancer screening. Out of 200 patients, maximum patients (41%) were in 31–40-year age group followed by 21–30-year age group (26%) in the present study. Minimum subjects were from the age group of 61-65 years (7%) followed by 51-60 years (table 1, graph 1).

Table 1: Age distribution among the study subjects

Age Group (in years)	N	%
21-30	52	26
31-40	82	41
41-50	36	18
51-60	16	8
61-65	14	7
total	200	100

Table 2: Residential status among the study subjects

Residential	N= 200	%
Rural	152	76
Urban	48	24

Majority of the subjects were from rural area (76%) in this study

Table 3: Clinical presentation among the study subjects

Parameters	N= 200	%
Routine health check up	96	48
Menstrual irregularities	27	13.5
Dysfunctional bleeding per vaginum	15	7.5
Pain lower abdomen	13	6.5
Lower urinary tract symptoms	10	5
Dyspareunia	3	1.5
Discharge per vaginum	37	16.5
Mass protruding per vaginum	2	1
Infertility	2	1

Table 3, shows the clinical presentation among the study subjects. 48% of the women came for routine health checkup. Most common clinical presentation among the study subjects was discharge per vaginum (16.5%) followed by menstrual irregularities (13.5%) and bleeding per vaginum (7.5%). Pain in lower abdomen and lower urinary tract symptoms was found in 6.5% and 5% of the women respectively.

Table 4: Cervical examination among the study subjects

Cervical Examination	N= 200	%
Normal	182	91
Erosion	15	7.5
Cervical mass and suspicious of carcinoma	3	1.5

Normal cervical examination was revealed in 91% of the women. Erosion and cervical mass with suspicious of carcinoma was reported in 7.5% and 1.5% of the women respectively (table 4, graph 4).

Table 5: Distribution of study subjects according to interpretation of conventional pap smear

CONVENTIONAL PAP SMEAR	N= 200	%
Unsatisfactory smear	14	7
NILM	22	11
Inflammatory smear	136	68
Atrophic smear	8	4
LSIL	6	3
Bacterial vaginosis	6	3
Atypical squamous/ glandular cells	3	1.5
HSIL	1	0.5
Fungal infection candidiasis	2	1
Trichomonas vaginalis	1	0.5
SCC	1	0.5

Conventional pap smear revealed unsatisfactory, NILM (Normal smear) and inflammatory smear among 7%, 11% and 68% of the subjects respectively. Atrophic smear, LSIL, bacterial vaginosis, Atypical squamous/Glandular Cells, HSIL, fungal infection (candidiasis), trichomonas vaginalis and SCC was reported among 4%, 3%, 3%, 1.5%, 0.5%, 1%, 0.5% and 0.5% of the women respectively

Table 6: Distribution of study subjects according to interpretation of LBC

LBC	N= 200	%
Unsatisfactory smear	0	0
NILM	32	16
Inflammatory smear	130	65
Atrophic smear	11	5.5
LSIL	11	5.5
Bacterial vaginosis	6	3
Atypical squamous/ glandular cells	4	2
HSIL	2	1
Fungal infection candidiasis	2	1
Trichomonas vaginalis	1	0.5
SCC	1	0.5

LBC showed unsatisfactory, NILM (Normal smear) and inflammatory smear among 0%, 16% and 65% of the subjects respectively. Atrophic smear, LSIL, bacterial vaginosis, Atypical squamous/Glandular Cells, HSIL, fungal infection (candidiasis), trichomonas vaginalis and SCC was reported among 5.5%, 5.5%, 3%, 2%, 1%, 1%, 0.5% and 0.5% of the women respectively (table 6).

Table 7: Correlation between interpretation of conventional pap smear and LBC

Finding	Conventional PAP Smear	LBC	KAPPA Value
Unsatisfactory smear	14	0	0
NILM	22	32	0.53
Inflammatory smear	136	130	0.81
Atrophic smear	8	11	0.79
LSIL	6	11	0.62
Bacterial vaginosis	6	6	1
Atypical squamous/glandular cells	3	4	0.92
HSIL	1	2	0.50
Fungal infection	2	2	1
Trichomonas vaginalis	1	1	1
SCC	1	1	1

LBC didn't reveal any unsatisfactory smear while PAP reported 14 unsatisfactory smears. Excellent correlation was found between LBC and Conventional pap smear w.r.t. inflammatory smear, atrophic smear, bacterial vaginosis, Atypical squamous/Glandular Cells, fungal infection (candidiasis), trichomonas vaginalis and SCC.

Premalignant lesions (LSIL, HSIL) in the form of dyskaryotic changes were observed in pap smear i.e., LSIL 3%, HSIL 0. 5% of the patients. (Table 7, graph 7).

1 cases of frank malignancy were detected. The smear contained many malignant squamous cells with evidence of intracellular keratinization displaying high nuclear/ cytoplasmic ratio, coarse chromatin with moderate amount of cytoplasm. Many fibre cells with hyperchromatic ovoid nuclei, which are diagnostic of invasive carcinoma were also observed.

4. Discussion

The Conventional pap smear has been utilized for cervical cancer screening for more than 50 years. Despite being credited with a 70% reduction in mortality for cervical cancer, the false negative rate is still a cause for concern. It is widely acknowledged that 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[49]. Both conventional pap and liquid based cytology was performed in the same patient. The aim of the study was to compare conventional pap smear and Liquid based cytology for cervical cancer screening. The findings of the study are Maximum patients (41%) were in 31–40-year age group followed by 21–30year age group (26%) in the present study. Majority of the subjects were from rural area (76%) in this study. In the present study, 48% of the women came for routine checkup. Most common clinical presentation among the study subjects was discharge per vaginum (16.5%) followed by menstrual irregularities (13.5%) and bleeding per vaginum (7.5%). Pain in lower abdomen and lower urinary tract symptoms was found in 6.5% and 5% of the women respectively. Normal cervical examination was revealed in 91% of the women. Erosion and cervical mass with suspicious of carcinoma was reported in 7.5% and 1.5% of the women respectively. Conventional pap smear revealed unsatisfactory, NILM (Normal smear) and inflammatory smear among 7%, 11% and 68% of the subjects respectively. Atrophic smear, LSIL, bacterial vaginosis, Atypical squamous/Glandular Cells, HSIL, fungal infection (candidiasis), trichomonas vaginalis and SCC was reported among 4%, 3%, 3%, 1.5%, 0.5%, 1%, 0.5% and 0.5% of the women respectively. LBC showed unsatisfactory, NILM (Normal smear) and inflammatory smear among 0%, 16% and 65% of the subjects respectively. Atrophic smear, LSIL, bacterial vaginosis, Atypical squamous/Glandular Cells, HSIL, fungal infection (candidiasis), trichomonas vaginalis and SCC was reported among 5.5%, 5.5%, 3%, 2%, 1%, 1%, 0.5% and 0.5% of the women respectively. LBC didn't reveal any unsatisfactory smear while PAP reported 14 unsatisfactory smears.

5. Conclusion

LBC can be a better alternative to conventional smear because of lower rate of unsatisfactory smears. Also, it has

advantages of less obscuring by blood, mucus material and inflammatory cells. Liquid based cytology, inspite of its increased cost, 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 lesions

Conflict of Interest: Nil

References

[1] Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global Cancer statistics. CA Cancer J Clin 2011; 61: 69-90.
[2] Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C et al. GLOBOCAN 2012 V1.0 Cancer incidence and Mortality Worldwide: IARC
[3] Cancer Base no. 11. Lyon, France. International Agency for Research on Cancer; 2013. Available at http://globocan.iarc.fr.
[4] International Agency for Research on Cancer Global Cancer Observatory. http:// gco.iarc.fr/today/data/factsheets/populations/356-india-fact-sheets.pdf.
[5] Last Accessed on 15th August, 2021.
[6] Centers for Disease Control and Prevention. Global Cancer Statistics. http://www.cdc.gov/cancer/international/statistics.htm. Accessed May 13, 2021
[7] World Health Organization. Human papillomavirus (HPV) and cervical cancer. http://www.who.int/mediacentre/factsheets/fs380/en/. Accessed June 10, 2021.
[8] American Cancer Society. Global Cancer Facts & Figures. 2nd ed. http://www.cancer.org/acs/groups/content/@epidemiol ogysurveilance/docume nts/document/acspc-027766.pdf. Accessed June 10, 2021.
[9] Surveillance, Epidemiology, and End Results. SEER Stat Fact Sheets: cervix uteri cancer. http://seer.cancer.gov/statfacts/html/cervix.html. Accessed July 26, 2021.
[10] Landoni F, Maneo A, Colombo A, et al. Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. Lancet. 1997; 350:535-
[11] 540.
[12] Gadducci A, Sartori E, Maggino T, et al. The clinical outcome of patients with stage Ia1 and Ia2 squamous cell carcinoma of the uterine cervix: a
[13] Cooperation Task Force (CTF) study. Eur J Gynaecol Oncol. 2003; 24:513516.
[14] Sedlis A, Bundy BN, Rotman MZ, Lentz SS, Muderspach LI, Zaino RJ. A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: a Gynecologic Oncology Group Study. Gynecol Oncol. 1999; 73: 177-183.
[15] Morris M, Eifel PJ, Lu J, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for highrisk cervical cancer. N Engl J Med. 1999; 340: 1137-1143.
[16] Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. N Engl J Med. 1999; 340: 1144-1153.
[17] Whitney CW, Sause W, Bundy BN, et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. J Clin Oncol. 1999; 17: 1339- 1348.
[18] Eifel PJ, Winter K, Morris M, et al. Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation for highrisk cervical cancer: an update of Radiation Therapy Oncology Group trial (RTOG) 90-01. J Clin Oncol. 2004; 22: 872-880.
[19] Rose PG, Ali S, Watkins E, et al. Gynecologic Oncology Group. Long-term follow-up of a randomized trial comparing concurrent single agent cisplatin, cisplatin-based combination chemotherapy, or hydroxyurea during pelvic irradiation for locally advanced cervical cancer: a Gynecologic Oncology Group Study. J Clin Oncol. 2007; 25: 2804-2810.
[20] Keys HM, Bundy BN, Stehman FB, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. N Engl J Med. 1999; 340: 1154-1161.
[21] Stehman FB, Ali S, Keys HM, et al. Radiation therapy with or without weekly cisplatin for bulky stage 1B cervical carcinoma: follow-up of a Gynecologic Oncology Group trial. Am J Obstet Gynecol. 2007; 197:503. e1-e6.
[22] Potter R, Georg P, Dimopoulos JC, et al. Clinical outcome of protocol-based image (MRI) guided adaptive brachytherapy combined with 3D conformal radiotherapy with or without chemotherapy in patients with locally advanced cervical cancer. Radiother Oncol. 2011; 100: 116-123.
[23] Whitlock EP, Vesco KK, Eder M, et al. Liquid – based cytology and human papillomavirus testing to screen for cervical cancer. A systematic review for the US preventive services Task Force. Ann Intern Med 2011; 155:687.
[24] Senapathy JG, Umadevi P, Kannika PS. The present scenario of cervical cancer control and HPV epidemiology in India: An outline. Asian Pac J Cancer Prev 2011; 12: 1107-15.
[25] Gakidou E, Nordhagen S, Obemeyer Z. Coverage of cervical cancer screening in 57 countries: low average levels and large inequalities. PLOS Med 2008; 5: e132.
[26] Dasari P. A grossly abnormal cervix: Evidence for using colposcopy in the absence of a squamous intraepithelial lesion by the conventional Papanicolau's test. Journal of Gynecologic Surgery. 2011 March; 27(1):5-8.
[27] Papanicolaou GN. Introduction of Pap smear in early detection of cervical malignancies. Am J Clin Path 1940; 19: 301-8.
[28] Park IA, Lee SN, Chaw SW, Kim JW. Comparing the accuracy of thin prep pap tests and conventional pap smears on the basis of the histologic diagnosis - a clinical study. Acta Cytol 2001; 45: 525-31.

[29] Hutchinson ML, Agarwal P, Denant T, Cibas E. A new look at cervical cytology: thin prep multicenter trial results. Acta Cytol 1992; 36: 499-54.
[30] Bolick DR, Hellman DT. Laboratory implementation and efficacy assessment of the thin prep cervical cancer screening system. Acta Cytol 1998, 42: 209-13.
[31] Guo M, Hu L, Martin L, Liu S, Baliga M, Hughson MD. Accuracy of liquidbased Pap tests: comparison of concurrent liquid-based tests and cervical biopsies on 782 women with previously abnormal Pap smears. Acta Cytol. 2005; 49(2): 132-8.
[32] Karnon J, Peters J, Platt J, Chilcott J, McGoogan E, Brewer N. Liquid-based cytology in cervical screening: an updated rapid and systematic review and economic analysis. Health Technol Assess. 2004; 8(20): iii,1-78.