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Original Research Article

Comparative study of PAP smear and colposcopy with cervical biopsy

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ABSTRACT

Background: Cervical Cancer is the second most common cancer among women worldwide approximately 80% of which occurred in developing countries. Out of all cervical cancer cases seen in the world, only 14% are in the developed countries, while about 86% occurs in the developing countries. The Cervical cancer is the leading cause of cancer in Indian women. Cervical cancer is usually preceded by a long phase of cytological changes, known as cervical intraepithelial neoplastic (CIN) and takes a long period of 15-20 years before the invasive cancer develops". Thus cervical cancer can be prevented if cellular changes are detected and treated in early stage. World Health organization considers cervical cancer as a preventable disease. This is because it can be diagnosed in its precancerous phase. So we have done study to study efficacy of pap smear and colposcopy. Comparative study of PAP smear and colposcopy with cervical biopsy in women with symptomatic/ unhealthy cervix.
Methods: All the high risk women of reproductive, perimenopausal and postmenopausal age group who presented with unhealthy cervix on naked eye examination, abnormal vaginal discharge, post coital bleeding, intermenstrual spotting/bleeding, cervix that bleeds on touch and abnormal uterine bleeding. An informed consent was obtained before performing Pap's smear and colposcopy. In case there was abnormal cytology report, the patient's cervical biopsy was done.
Results: The sensitivity of Pap smear is 50%, specificity is 86.6%, positive predictive value (PPV) 37.8%, and negative predictive value is 91.4%. The sensitivity of coloposcopy smear is 96.4, specificity is 39.53 and positive predictive value (PPV) 20.61%, negative predictive value is 98.55%.
Conclusions: Colposcopy is definitely more sensitive and accurate than pap smear. By combining Pap smear with colposcopy, we can maximize the sensitivity and specificity of cancer cervix screening.

Keywords: Cervical biopsy, Colposcopy, Pap smear, Unhealthy cervix

INTRODUCTION

Cervical cancer is currently projected to be the fourth most frequent disease in women globally, as well as the primary cause of cancer mortality in some of the world's poorest nations. Only approximately 20% of women in LMICs have ever been tested for cervical cancer, compared to more than 60% in high-income countries. Among 2018, 290 000 (51%) of the 570 000 new cervical cancer cases globally occurred in women living in LMICs (500 000 [88%] when includes upper-middle-income countries).[1,2] In 2015, India had the highest recorded age-standardized death rate of 16/100,000/year. Tobacco use, the number of sexual partners, and a family history of cervical cancer have all been identified as important risk factors.[3]

The implementation of systematic call and recall screening programs has resulted in a significant decrease in cervical cancer incidence and death.[4] This is due to the ability to diagnose and treat pervasive precursors [cervical intraepithelial neoplastic (CIN)].[5] Cervical cancers can be

avoided with HPV vaccine (primary prevention for pre-adolescent and young teenage females) and cervical screening (secondary prevention for women).

In 2014, organized and thorough cervical screening procedures resulted in projected rates of HPV vaccination uptake in young teenage females of more than 30% in affluent nations but fewer than 3% in less-developed regions.[6]

Before advancing to invasive cancer, cancer cervix has a protracted phase of pre-invasive illness that proceeds from cellular atypical to different degrees of dysplasia or cervical intraepithelial neoplastic. Factors such as easy cervix accessibility, proclivity of cervical epithelial cells to exfoliate, rapid turnover of epithelial cells, a broad spectrum of histopathological changes, and a long natural history of disease provide the best potential for disease progression control through population screening.

A PAP smear is a cytological examination of exfoliated or scraped cells that is used to identify dysplasia. Visual inspection of the cervix with acetic acid (VIA) is a simple screening approach that involves applying 3-5% acetic acid to the cervix and searching for aberrant aceto-white patches indicative of dysplasia or invasive illness. VILI is a visual examination of the cervix with Lugol's iodine to locate Schiller's light zones in order to test for pre-invasive illness. VIA and VILI are both simple to conduct and understand, even for paramedics with adequate training. The squamo-columnar junction and Transformation zone are detected using colposcopy, and acetic acid is then utilized to analyze the specifics of any lesion and labeled according to IFCPC (International Federation for Cervical Pathology and Colposcopy). Target biopsies can be performed on abnormal locations, and lesions can be treated while retaining fertility.

METHODS

This study was a prospective observational comparative study. The study conducted at Department of Obstetrics and Gynaecology, Sri Aurobindo Institute of Medical Sciences for 18 months (April 2021 to September 2022) after the approval of Ethics Committee.

Inclusion criteria

All the high-risk women of reproductive, perimenopausal and postmenopausal age group who presented with the unhealthy cervix on naked eye examination (hypertrophied cervix, cervical ectropion, any cervical growth), abnormal vaginal discharge and post coital bleeding intermenstrual spotting/bleeding cervix that bleeds on touch abnormal uterine bleeding were included in this study.

Exclusion criteria

Women with bleeding per vaginum at the time of examination, women with frank invasive cancer, women who underwent hysterectomy, pregnant women, patients not giving consent for study were excluded in this study.

Detailed history of the women included age, presenting complains, obstetric outcome, marital history/number of partners and use of contraceptives. We also took into account age at first intercourse and age at marriage. Family history, socioeconomic history and personal (hygiene and addictions to smoking and drug) were also taken. After obtaining the history, a general physical examination and systemic examination was carried out. Per speculum examination was performed to note any abnormality on direct visual inspection of the cervix without magnification. Abnormal finding were noted. Both pap and colposcopy done

In case there was abnormal cytology report, the patient's cervical biopsy were done. Histopathology is the gold standard for cervical cancer. Abnormal Pap's smear and colposcopy co-related with danced cervical biopsy.

Methodology

After explaining the procedure, the patient laid comfortably in dorsal position Light was positioned to visualise the cervix clearly. Sims speculum and anterior wall of vagina retracted by anterior vaginal wall retractor, cervix brought into view by gentle movement of the speculum encouraging the patient to relax appearance of cervix was noted. To obtain an adequate sample of the al de Ayre's spatula was 360 degrees, clockwise and anti-clockwise, keeping if firmly attached to the cervix. The device should be turned at least 3-5 times. The material obtained was smeared evenly on a glass slide into a bottle containing 10%.

The cervical smear stained with papaniculao technique and then reported according to the Bethesda system. Cytology considered positive if it revealed any of the following atypical Squamous Cells of Undetermined significance (SCUS ASC-H. Low Grade Squamous Intraepithelial lesion (SI L), High Grade Squamous Intraepithelial lesion (HSI) or cells suspicion of malignancy. Negative smears included those with an inflammatory report. Then colposcopy was performed using video colposcope in all women, colposcopy was done according to conventional method and Modified Reidscolposcopic index (RCI) was performed. The cervix was visualized under low power to note any abnormal findings.

Capillaries and surface blood vessels of the cervix were visualized under low power to note any abnormal findings capillaries and surface blood vessels were examined with a green filter. 3-5% glacial acetic acid was gently applied twice over the cervix for a total period of one minute, to ensure appropriate acetowhite reaction. Transformation Zone was defined between the old and the new squamo-columnar junctions. Colposcopy considered unsatisfactory if the new squamo-columnar junction is not visualised and endo-cervical curettage will be performed. The

colposcopy Reids scoring method. Examination of each quadrant was done in clockwise direction, acetowhite reaction was seen in the transformation zone; then margin, colour, vessels and colposcopy applied and findings were documented.

Reids colposcopic scoring/index was done. Lugols iodine did not stain the acetowhite area. Colposcopic guided biopsies were taken with punch biopsy from the site with highest score and transferred to vial containing formaldehyde and sent for histopathology examination colposcopy was recorded separately (endocrocal p obtained from all the women for analysis). Cervical biopsy is the gold standard for detection of cervical cancer all the abnormal cytological findings on Pap's smear was subjected to colposcopy and directed cervical biopsy.

Statistical analysis

All results were compiled and subjected to statistical analysis. Data was entered into Microsoft excel and SPSS (Statistical package for social science) version 23.0 was used for descriptive statistics. The sensitivity, specificity, predictive value of positive test, predictive value of negative test, percentage of false positives and percentage of the negative was calculated.

RESULTS

In this study, 33% women belong to age group 41-50 years. 23% women belong to 51-60 years of age. 2% women belong to 20-30 years of age, 22% women belong to 31-40 years of age and 20% women are more than 60 years of age. In this study there were 2 % with parity 1, 21% with parity 2, 29% with parity 3, 26 with parity 4, 9 % with parity 5, 7% with parity 6, 5% with parity 7 and 1 % with parity 8.

Table 1: Distribution according to PAP smear findings.

PAP smear findings	Number	Percentage
Inflammatory	79	79
LSIL	1	1
HSIL	3	3
ASCUS	15	15
Vaginosis	2	2
Total	100	100

Majority of the women 54 % got married in the age 15- 20 years, 15% got married in the age 21-25 years, 14% got married in the age <15 years, 10 % got married in the age 26-30 years, 3% got married in the age 31-35 years, 3% got married in the age 40 years. 36-40 years and only 1 got married in the age more than 40 years.

In this study population, majority 60 % presented with white discharge, 15% presented with post-coital bleeding, 11% each of irregular cycles and intermenstrual bleeding, 8% were asymptomatic, 6 % each presented with pain in abdomen and postmenopausal bleeding, 1% presented with dyspareunia and 4% presented with other complaints.

In present study the per vaginum findings 59% bulky uterus was seen while in 41 % women it was normal.

In this study, PAP smear has showed maximum 79% women having inflammatory, in 1 it showed LSIL, in 3% HSIL was the finding, in 15% it showed ASCUS and in 2% findings were suggestive of bacterial vaginosis (shown in Table 1).

Table 2: Distribution according to colposcopy findings.

Colposcopy findings	Number	Percentage
Aceto white area	34	34
Metaplasia	35	35
Mosaic pattern	5	5
Punctate	8	8
Abnormal vascularity	9	9
Polyp	5	5
Growth	4	4
Total	100	100

In this study, authors found that colposcopy showed 34% acetowhite area, 35% metaplasia, 5% mosaic, 8% punctuate, 9% abnormal vascularity, 5% polyp, and in 4% the findings were suggestive of polyp/growth (shown in Table 2).

In this study, authors found that histopathological findings showed in 85% chronic cervicitis, 2% it was CIN-1, in 3% chronic cervicitis with carcinoma in situ, 1 well differentiated squamous cell carcinoma, in 5% it was moderately differentiated squamous cell carcinoma grade 1, in 6% it was moderately differentiated squamous cell carcinoma grade 2 and in 1% features were suggestive of neuroendocrine tumor's (Table 3).

Table 3: Distribution according to histopathology report.

Histopathology findings	Number	Percentage
Chronic cervicitis	85	85.00
CIN-1	2	2.00
Carcinoma in situ	3	3.00
Well differentiated SCC	1	1.00
Moderately differentiated SCC	8	8.00
Neuro endocrine tumor's	1	1.00
Total	100	100

The sensitivity of Pap smear is 50%, specificity is 86.6%, Positive predictive value (PPV) 37.8%, and negative predictive value is 91.4% (Table 4).

Table 4: Results of Pap smear.

		Histopathology finding		Total
		Positive	Negative	
Pap smear	Positive	07	12	19
	Negative	07	74	81
Total		14	86	100

The sensitivity of coloposcopy smear is 96.4, specificity is 39.53, Positive predictive value (PPV) 20.61%, negative predictive value is 98.55% (Table 5).

Table 5: Results of colposcopy smear.

		Histopathology finding		Total
		Positive	Negative	
Colposcopy	Positive	13	52	65
	Negative	01	34	35
Total		14	86	100

The chi- square (x^2) value obtained was 91.012 with a degree of freedom of 42; the P value obtained was 0.0001, which is statistically significant. Thus, there is a strong association between histopathology findings and parity. The chi- square (x^2) value obtained was 67.591 with a degree of freedom of 36; the P value obtained was 0.0011, which is statistically significant. Thus, there is a strong association between histopathology findings and age at marriage. The x^2 value obtained was 102.586 with a degree of freedom of 24, the P value obtained was 0.0001, which is statistically significant. Thus, there is a strong association between histopathology findings and papanicolaou findings. The x^2 value obtained was 189.743 with a degree of freedom of 36; the P value obtained was 0.0001, which is statistically significant. Thus, there is a strong association between histopathology findings and colposcopy findings. The x^2 value obtained was 70.077 with a degree of freedom of 24, the P value obtained was <0.05, which is statistically significant. Thus, there is a strong association between colposcopy findings and papanicolaou findings.

DISCUSSION

Unhealthy cervix is a group of cervical lesions, mostly chronic which includes chronic cervicitis, endocervicitis, cervical erosions, lacerations polyps and leukoplakia. These conditions can harbor pre malign lesions. When a gynecologist encounters any of these conditions, it is necessary to evaluate them in most purposeful manner to rule out any premalignant lesion.

Frequently repeated cytology screening programs have led to a large decline in cervical cancer incidence and mortality in developed countries. Cytology based screening programs have achieved very limited success in developing countries like ours due to lack of trained personnel, laboratory facilities, equipment's, high cost of services and poor follow-up. It has become necessary to find out alternative screening procedure to cytology which has high sensitivity and specificity.

The present study was conducted on 100 patients attending the outpatient with clinical diagnosis of unhealthy cervix. papaniculie smear was taken for all patients. For confirmation of Pap smear report all women underwent colposcopic examination and biopsies were taken in the unhealthy cervix. Final diagnosis was made according to the histopathology reports.

In this study, maximum patients (32.50%) belonged to age group 41-50 year study, Which is inconsistent with study of Indu et al, Kalyankar et al, Shaki et al and Thobbi et al where maximum patients were in the age group of 31-40 years.[7-10] This could be attributed to the higher age at which are patients came symptomatically and presented with complains to warrant screening at OPD.

Majority of cases with abnormal cervical lesions were in the multiparous women (parity 2 to 4) which constituted 152 (76%) cases out of 200 cases. In our study we found a significant association between parity and histopathology. None of the cases of neoplastic lesion was seen in nulliparous or primiparous women. Which was consistent with study of Kaveri et al, Kushtagi et al, Kalyankar et al and Vaidya et al also showed that prevelance of unhealthy cervical lesions was significantly higher in parity more than 2 and parity more than 4 respectively.[11,12,8,13] The correlation of multiparity and cervical neoplasia may be attributed to hormonal and nutritional changes that occur in pregnancy, immunosuppression during pregnancy, and cervical trauma during vaginal delivery.

In our study, majority of women with unhealthy cervix were married at age 15-20 years 53 out of 100 women. We found significant association of histopathology in relation to age at marriage. This was supported by Kushtagi et al, Sherwani et al, Manjith et al, Verma et al, Kaveri et al who demonstrated that the severity of underlying CIN increased with increase in the duration of marital life and hence the increase in the duration of exposure to sexual intercourse.[12,14,15,7,11]

Majority of patients in our study presented with complains of white discharge 60 out of 100 women. Followed by complains of post coital bleeding 15, irregular menstrual cycles 11 and intermenstrual bleeding 11. Similar to studies done by various authors where white discharge was most common presenting complaint Ramesh et al, Verma, Kaveri et al, Manjit et al, Sachan et al, Vincent et al.[16,15,17,18]

In the present study majority of patients had hypertrophy of cervix 46% as gross appearance of cervix followed by erosion 40% and congested cervix 10.5%. Findings in study by Padambhan et al, erosion in 31.25%, hypertrophied cervix in 23.75 %, Indu et al with finding of hypertrophied cervix which bled on touch (17.65%) and

erosion (17.65%).[19,7] This is in contrast to study by Kaveri et al which showed erosion 51.7% which was followed by growth in 27.5% cases followed by hypertrophy in 20%.

According to our study significant association was seen between papanicolaou findings and histopathology. significant association was also seen between the findings of colposcopy and histopathology as well as between colposcopy and papanicolaou findings. Pap smear showed 79 women having inflammatory with acterial vaginosis in 2, in 1 it showed LSIL, in 3 HSIL was the finding, and in 15% it showed ASCUS. No patients with ASC-O and AGUS were found in our study. Few patients had growth but Pap smear could not detect invasive lesion in them. This could be because Pap smear may not have picked up carcinoma cells but HSIL. Similar findings were seen in study by Indu et al which showed epithelial cell abnormality in 17 out of 122 smears (13.6%) and 68.80% smears negative for intraepithelial lesions and malignancy. In the study by Ashmita et al, 82.7% women had normal (or inflammatory) pap smear while 3.8 % had HSIL which was consistent with our study.[20]

In our study, in colposcopy acetowhite area was found in 34% metaplasia in 35%, mosaic in 5%, punctuate in 8%, abnormal vascularity in 9%, polyp in 5% and growth was seen in 4% patients. Study by Ashmita et al, colposcopy suggestive of low-grade infection in 55.8% and high grade or suspicious of malignancy in 22.5% women.[20] According to Ramesh et al, colposcopy showed acetowhite areas in 36% punctuations in 40% mosaic pattern 16%, abnormal vascularity in 8%.[16] Study by Suguna et al on colposcopy 18% were normal 46% had squamous metaplasia, 32% had atypical transformation zone, 1% had frank invasion.

In our study, according to histopathology, 85% patients had chronic cervicitis, CIN1 was seen in 2%, chronic cervicitis with carcinoma in situ 3%, well differentiated squamous cell carcinoma in 1% and moderately differentiated carcinoma in 8%. In study by Ashmita et al, final histopathological study correlated with diagnosis of CIN in 3.8% and chronic cervicitis with metapasia in 63.5%. In the study by Suguna et al, biopsy showed 5% were normal, 30% showed chronic cervicitis, 19% had metaplasia, 32% had dysplasia 3.22% had invasive cancer.[20,21]

Sensitivity of Pap smear in our study was 50% Specificity of Pap smear was 86.62%. Positive Predictive Value of Pap Smear (PPV) was 37.83% Negative Predictive Value of Pap Smear (NPV) was 91.41% for colposcopy; sensitivity in our study was high as 96.27%. but was found to be low as 39.53% specificity, PPV was found to be 20.61%, NPV was 98.55%. In the study by Ashmita et al, overall pap smear had a poor, sensitivity compared to colposcopy 19.5% Vs. 90.24% respectively.[20] In the Study by Suguna, sensitivity of colposcopy was 95%, specificity was 60%, FNV- 2%.[21] In the study by Ramesh et al, sensitivity of colposcopy was 83.3% comparable to study done by Singh et al where it was 91%.[16,22]

According to Richa et al, sensitivity of Pap smear was 25.40%, specificity was 99.27%, Richa et al PPV for Pap smear was 94.12%, NPV was 74.32%.[23] Richa et al sensitivity of colposcopy was 79.37%, specificity was 81.02% Richa et al colposcopy - PPV was 65.79%, NPV was 89.52%.[23] With above discussion we can conclude colposcopy is definitely more sensitive and accurate than Pap smear.

Study should have been done in vast population at community level rather than a single center level. This was the limitation of this study.

CONCLUSION

Colposcopy is definitely more sensitive and accurate than pap smear. By combining Pap smear with colposcopy, we can maximize the sensitivity and specificity of cancer cervix screening.

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