

A comparative Study to Assess the Accuracy of Colposcopic Examination and Pap Smear Cytology As Screening Test In Unhealthy Cervix

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Abstract: It was a prospective comparative study conducted in gynecology OPD of Burdwan Medical College and Hospital on 100 women attending OPD with complains of white discharge, irregular menstruation, post coital bleeding or post-menopausal bleeding. Pap smear, colposcopy with application of 3% acetic acid and on spot cervical biopsy in indicated cases was done. 71% of women were in the age group 20-40 years. 54% had parity of 3 to 4. 69% of women presented with complain of white discharge. 88% had normal Pap smear, 1% had LSIL, 2% had HSIL and 4% had ASCUS on Pap smear. 40% of women had aceto- white reaction on colposcopy, 6% had low grade lesions and 54% had normal colposcopy findings. Final histopathology correlated with a diagnosis of CIN 2/3 in 6%, CIN 1 in 1% and squamous cell carcinoma in 4%, while 89% had chronic nonspecific cervicitis. 72.72% of all those with a positive histopathology presented with complain of white discharge and positivity increased as the parity increased. Overall sensitivity of Pap smear was 72.72% which was much lower as compared to colposcopy (100%). But the specificity of Pap smear was 95.5% and of colposcopy was 67.42%. Hence colposcopy is a superior test for the screening of cervical cancer as it is more sensitive than Pap smear in detecting precancerous lesions.

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I. Introduction

Cervical cancer is the second most common cancer after the cancer breast¹ and the 5th deadliest cancer in women worldwide. An estimated 4,70600 new cases occur among women each year worldwide². Approximately 80% of cervical cancer occurs in developing countries² of which India contributes to about 20-30% of the global burden³. In India it is the most common cancer among women and is the leading cause of cancer death in Indian women. It kills around 73,000 women in India every year. While it is the 5th leading cause of mortality in the developed countries due to the availability of the Pap smear and rapid response – surgically and medically. Another reason for the difference is the availability of HPV vaccines freely outside the 3rd world as the HPV is found in over 90% of women diagnosed with cervical cancer.

WHO considers cervical cancer as a preventable disease. This is because it can be diagnosed in its pre-cancerous phase⁴. So considerable efforts have been given into detecting and treating it in its pre-invasive stage all over the world. Precancerous lesions occur more commonly in women less than 40 years of age which provide opportunity for screening and early detection of cervical cancer⁵. In most developed countries, screening programs for early detection of pre-clinical cervical cancer have proven to be very useful and have contributed

to improved results of treatment. PAP smear and colposcopy are the principal methods used in early detection of cervical cancer.

Cervical cancer, leads to significantly fewer deaths when effective early detection methods are available, either via a Pap smear or with a test for presence of the human papilloma virus (HPV). However, such tests aren't readily available to many women in low-resource settings, and even for those women with access to health care services, compliance with recommendations for testing is not assured.

If cervical cancer is detected early, it often can be cured. Conversely, for those women who present with late-stage disease, there remains a need for better therapies. NCI (National cancer Institute) have sponsored a clinical trial that will have an important impact on the treatment of late-stage disease, and also having funded a screening trial in India using a network of community outreach workers to offer low tech-screening VIA, by direct visual inspection of the cervix coated with dilute acetic acid (vinegar).

Pap smear is a test that requires trained cytologists to examine the cells retrieved from the cervix and consistently identify samples that are abnormal. Shastri's study looks at the less sophisticated technique of VIA that relies on direct visualization of the cervix after it is swabbed with vinegar. His challenge was not only to identify a test that works, but also to find a method to get the test to women in communities where health care facilities and transportation may present challenges.

In the trial, local health workers and community residents were identified and trained to provide VIA to women who needed screening. More than 75,000 women from 10 communities had multiple rounds of VIA. The screened women were compared to over 76,000 women from 10 similar communities where women were informed about cancer risks and the available screening facilities, were given vouchers for free cervical cancer screening at Tata Memorial hospital, but were not offered the outreach system with VIA performed by community health workers. The trained outreach workers also helped ensure that women with abnormalities were escorted to Tata Memorial hospital, where they underwent re-examination with colposcopy (which uses a tool to provide an illuminated, magnified view of the cervix) and then received appropriate diagnostic testing and treatment. The findings from this study showed that the community screening group had a 31 percent reduction in death due to cervical cancer, which is significant.

The success of this trial in reducing death can be attributed to the combination of the VIA test and the outreach system, Shastri's team developed. Interim results from this study were published in the International Journal of Cancer⁶.

Colposcopy vs pap smear:

In all developed countries and in some developing countries Pap smear test has become a routine procedure for every gynecological patient for detecting of CIN and cervical cancer and it remains the most commonly used screening method for early detection of cervical cancer. It was introduced by George Papanicolaou into clinical practice in 1940⁷. In 1945 papanicolaou smear received the endorsement of the American Cancer Society as an effective method for the prevention cervical cancer. Centre of Cytology in Vancouver, BritishColumbia published data which confirmed that cytological screening leads to a reduction in the rate of invasive cancer of cervix. Park-et-al⁸ established that the sensitivity of the conventional Pap smear for the detection of cervical cancer precursors was less than 50%. Several limitations of conventional smear were identified including inadequate transfer of cells to slide⁹, inhomogeneous distribution of abnormal cells, inflammation or thick areas of overlapping epithelial cells. It also has the disadvantage of delay in providing immediate result.

WHO has recommended once in a life time screening for early detection of cervical cancer (ideally done every 3 years), in all women between 35 to 40 years of age¹⁰. Therefore it becomes important to use an adjunctive screening test like colposcopy which has high sensitivity (64-99) %¹¹, according to WHO, and can provide immediate results for evaluation of cervical precancerous lesions. Colposcopy further helps in executing a targeted biopsy which can be useful in defining diagnosis of precancerous lesions and cervical cancer¹².

Colposcopy was developed in 1925 by the German physician Hans Hinselmann, with help from Helmut Wirth¹³. It is a clinical method of detection of cervical cancer and CIN. Colposcope is a binocular microscope used for direct visualization of cervix. The interest in colposcope has developed only recently, may

be due to erroneous previous concept that exfoliative cytology of cervix renders colposcopy unnecessary, whereas colposcopy and cytology should correctly be regarded as complementary to each other.

It was stated in Krutzen and Ratnam that colposcopy complements cytology and when combined with selective biopsy, of the worst affected area, allows a high level of diagnostic accuracy of 90.7%¹⁴ and 95%¹⁵ respectively. Using cytology for screening and colposcopy for directing biopsy, a joint accuracy of approximately 90% to 99% can be achieved.

II. Materials And Methods

1. Study design: The study was a Prospective and Comparative study.

2. Study area: The study was conducted in Gynecology OPD of Burdwan Medical College and Hospital.

3. Study population: The study was conducted on women attending Gynecology OPD with complain of bleeding per vagina, post coital bleeding or any abnormal finding on per speculum examination.

Inclusion criteria:

1. Women having unhealthy cervix on per speculum examination.
2. Able to provide informed consent.
3. Age above 30 years.
4. Willing and able to follow study procedures & come to study center for study visits as described in the protocol
5. Expects to continue living in an area accessible to the study center for the duration of the study

Exclusion Criteria:

1. Pregnant women
2. Women having frank growth on cervix

4. Study period: one year (approximately)

5. Sample size: above 100

6. Procedure methodology: During the initial evaluation, a medical history was obtained. In some cases, a pregnancy test was performed before the procedure. The procedure was fully described to the patient, questions were asked and answered, and the patient then signed a consent form. A structured pro forma was prepared for each case which included informations regarding patients' age, chief complain, menstrual history, parity, findings per speculum and general physical examination.

During the speculum examination a Pap smear was taken. The smear was sent to Pathology department in koplins jar, where cytological examination was carried out on the smear prepared by conventional Papanicolaou method. The result of Pap smear was classified under two categories: - non-malignant and pre-malignant. The non-malignant category included normal smears and smears with inflammatory changes. The pre-malignant category is divided into 3 groups: - **HSIL**(High grade Squamous Intraepithelial Lesion), **LSIL**(Low grade Squamous Intraepithelial Lesion) and **ASCUS**(Atypical Squamous Cells of Undetermined Significance).

The patient was then subjected to colposcopy examination. The clinical methods and criteria as recommended by Coppersley was used. Colposcopy was performed in the dorsolithotomy position. A speculum was placed in the vagina after the vulva was examined for any suspicious lesions. 3% acetic acid was applied to the cervix using cotton swabs. Areas of acetowhitening correlate with higher nuclear density. The squamocolumnar junction, or "transformation zone", is a critical area on the cervix where many precancerous and cancerous lesions most often arise. Areas of the cervix which turned white after the application of acetic acid or had an abnormal vascular pattern was considered for biopsy. If no lesion was visible, an iodine solution was applied to the cervix to help highlight areas of abnormality. The colposcopically directed biopsies were taken from all examined patients, by punch biopsy forceps from the most advanced part of lesion. Biopsy fragments were sent to pathology department in a sterile container containing formalin.

Colposcopic examination included:

- Direct examination of cervix with green filter and saline application.
- Examination of the cervix after test with 3% acetic acid, seeing the junction of squamous cell, erosion, papillary lesions, aceto-white areas and vascular design;
- Examination of the cervix after Lugol iodinetest in which normal squamous epithelium, which contains glycogen, turns brown.

Statistical analysis:

Simple formula to calculate sensitivity, specificity and positive predictive value, was applied manually to the data.

Table no. 1

Calculation of the sensitivity, specificity, positive predictive value, negative predictive value of Pap test

	Histology +ve	Histology -ve
Pap +ve	8	4
Pap -ve	3	85

Sensitivity of Pap test - $8/11*100 = 72.72\%$

Specificity of Pap test – $85/89*100 = 95.50\%$

PPV of Pap test – $8/12*100 = 66.66\%$

NPV of Pap test– $85/88*100 = 96.59\%$

Table No. 2

Calculation of the sensitivity, specificity, positive predictive value, negative predictive value of colposcopy

	Histology +ve	Histology -ve
Colposcopy +ve	11	36
Colposcopy -ve	0	53

Sensitivity of colposcopy – $11/11*100 = 100\%$

Specificity of colposcopy – $53/89*100 = 59.55\%$

PPV of colposcopy – $11/47*100 = 23.40\%$

NPV of colposcopy – $53/53*100 = 100\%$

Table no.2 shows that sensitivity of colposcopy is very high but has a low specificity. The probability that the subjects with a positive result on colposcopy truly have the disease is 23.40% while the probability that the subjects with a negative result on colposcopy truly don't have the disease is 100%.

III. Result

1. From our study it was found that 26% of women were between 18-29 years. 47% were between 30-40 years and 27% were between 41-60 years.
2. 34% of women had parity between 0-2, 54% had parity 3-4 and 11% of women had parity of 5-6. Only 1% of women had parity 7 or more.
3. 69% of women came with the chief complaint of white discharge. 10% of women had the complaint of irregular menstruation. 8% complained of post coital bleeding and 5% of women complained of post menopausal bleeding.
4. Among 100 women 12 were found to be Pap positive, 47 were found to be colposcopy positive and 11 were found to be positive on histology.
5. Among the Pap smear finding 88% had normal smear, 2% had HSIL, 1% had LSIL, 4% had ASCUS and 5% had SCC.

6. Among the colposcopic finding 40% had acetowhite change, 7% had low grade lesion and 53% had normal colposcopic result.
7. The histopathology findings were as follows: 1% was found to have CIN1, 6% had CIN2/3 and 4% had SCC squamous cell carcinoma).
8. 2% of women were found to be Pap positive but colposcopy negative while 37% were found to be colposcopy positive but Pap negative.
9. 4% were positive on Pap smear but negative on histology while 3% were positive on histology and negative on Pap smear.
10. 36% were found to be positive on colposcopy but negative on histology. On the other hand there was no case who was positive on histology, when negative on colposcopy.
11. Among those who were found to be positive on Pap smear (12), 8 had the chief complain of white discharge, 3 had complain of post-menopausal bleeding and 1 complained of post coital bleeding.
12. Among those who were found to be positive on colposcopy (47), 33 had the chief complain of white discharge, 5 had menstrual irregularity, 4 complained of post coital bleeding, 3 complained of lower abdominal pain and 2 complained of post-menopausal bleeding.
13. Among histology positive patients (11), 8 had the chief complain of white discharge, 2 complained of post-menopausal bleeding and 1 complained of post coital bleeding.
14. 9 out of 12 of the Pap positive cases had parity >3.
15. 32 cases out of 47 of the colposcopy positive patients had parity <=3.
16. 8 out of 11 cases of histology positive patients had parity >3.
17. 25 out of 47 cases of colposcopy positive patients were more than 30 years.
18. 8 out of 11 histology positive patients were also more than 30 years.
19. Sensitivity of the Pap test is 72.72% from the above result and specificity is 95.50%.
20. Positive predictive value of Pap test came out to be 66.66% and negative predictive value as 96.59%.
21. Sensitivity of colposcopy calculated is 100% with specificity of 59.55%.
22. Positive predictive value of colposcopy is 23.40% and negative predictive value is 100% as obtained from the study.

Table No. 3

Distribution of women according to Pap findings (n=100)

Pap finding	Number	Percentage
Normal	88	88
LSIL	1	1
HSIL	2	2
SCC	5	5
ASCUS	4	4

Table no. 3 shows that the most commonly Pap smear abnormality was found in women was squamous cell carcinoma.

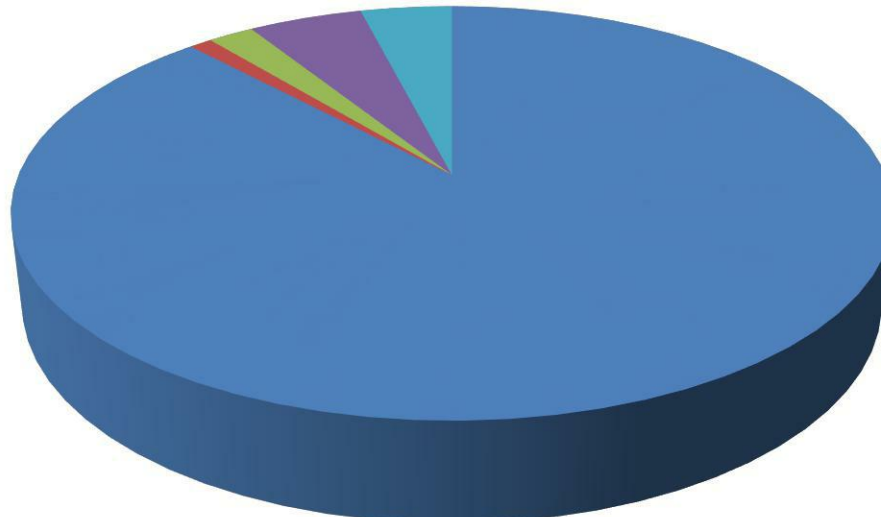
Table No. 4

Distribution of women to show relation between chief complain and Pap smear positivity

Chief complain	Pap +ve number	Percentage
White discharge	8	8
Post coital bleeding	1	1
Post-menopausal bleeding	3	3
Lower abdominal pain	0	0
Menstrual irregularity	0	0

Table 4 shows that most of the women who were pap positive had chief complaint of white discharge.

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No. 5
Distribution
women to
relation
between chief
complaint
colposcopy

Chief complain	Colposcopy +ve (number)	Percentage
White discharge	33	33
Post coital bleeding	4	4
Post menopausal bleeding	2	2
Lower abdominal pain	3	3
Menstrual irregularity	5	5

Table no. 5 shows that most of the patient whose colposcopy was positive had the chief complaint of white discharge

Table No.6
Distribution of women to show relation between chief complaint and histology

Chief complain	Histology positive Number	Percentage
White discharge	8	8
Post coital bleeding	1	1
Post-menopausal bleeding	2	2
Lower abdominal pain	0	0
Menstrual irregularity	0	0

Table no. 6 shows that most of the women with cervical cancer or pre-cancer had the complaint of white discharge.

IV. Discussions

From the above observations we can conclude that white discharge is a risk factor for cervical cancer and increasing parity is not very much related to the development of cervical cancer. It also becomes clear that increasing age is a risk factor for cervical cancer. All the women in the study belonged to low socio-economic strata and had married in early age. Thus it can also be concluded that low socio-economic status and early age of marriage (i.e sexual activity starting at an early age) are the risk factors for developing cervical cancer.

V. Conclusion

It can be concluded that colposcopy is a better screening test than Pap test for cervical cancer, because its sensitivity in detecting the precancerous and cancerous lesions of cervical cancer is more than that of Pap test. Colposcopy has more negative predictive value than Pap test, which means less number of cases will be missed by colposcopy and once the woman is screened negative by colposcopy, she has the least chance of having the disease. In our study, there were cases of under or over-diagnosis. The benefit of colposcopy and directed biopsy is to avoid over treatment of low-grade lesion, and under treatment of high-grade lesion. Colposcopy also has many advantages over Pap test, besides being more sensitive, it is also an outdoor procedure. It does not require any lab technician or qualified pathologist to know the result of the test, like in Pap test. It can be done by any person with proper training. Only disadvantage is the high cost of equipment. So, it can be done in remote villages by trained health worker. Thus we can rely on colposcopy for screening a mass population quickly and effectively to identify all those women who are at risk of developing cervical cancer.

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