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Correlation of Pap smearAnd Colposcopic Finding ofUnhealthy Cervix with Histopathology Report

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Abstract
Introduction:*Cervical cancer is a largely preventable disease, yet it remains the third most common cancer worldwide with over 5,30,232 (8.8%) new cases and mortality of 2,750,087(8.2%) annually.[1]The present study aims to compare and correlate colposcopy findings with pap smear taking histopathology as gold standard.*
Materials &Methods*:The present study is an observational prospective study whichwas carried out in Command Hospital AirForce (CHAF), Bangalore in Department of Obstetrics and Gynaecology.100 patients with unhealthy cervix attending the OPDwere selected who fit the inclusion criteria. Colposcopy and Pap smear were done in an unhealthy cervix and sensitivity, specificity, positive predictive value, negative predictive value and accuracy of both the methods were found out taking histopathology as gold standard.*
Results*:Out of 100 patients with unhealthy cervix evaluated. Pap smear was True positive in 9 cases, true negative in 80 cases, false positive in 3 cases, and false negative in 8cases. Thus, sensitivity of Pap smear was 52.94%, specificity of 96.38%, positive predictive value 75%, negative predictive value 90.9% and accuracy of 89%. Hence, Pap smear is less sensitive as a screening test.Colposcopy was true positive in 20cases, true negative in 71cases, false positive in 8 cases, and false negative in 1case. Thus, sensitivity of Colposcopy was 95.23%, Specificity 89.87%, positive predictive value 71.42%, negative predictive value 98.7% and Accuracy of 91%. Hence, colposcopy is more sensitive and accurate than Pap smear.*
Conclusion*:Pap smear is less sensitive and more specific compared to colposcopy. Colposcopy had more sensitivity and diagnostic accuracy as compared to Pap smear. Both Pap smear and colposcopy are complementary to each other. Hence, both Pap smear and colposcopy in a single visit is the better approach for detecting carcinoma cervix.*
Keywords:*Pap smear, Colposcopy, Cervix, Acetic Acid*

I. Introduction

Cervical cancer is a preventable disease, yet it remains the third most common cancer worldwide with over 5,30,232 (8.8%) new cases and mortality of 2,750,087(8.2%) annually.[1] Cancer in India accounted for 3.3% of the disease burden and about 9% of all deaths in 2004.[2]Further, the changing socio economic profile and initiation of different screening strategies have depicted a decline in the cervical cancer incidence and mortality worldwide.[3] The conventional Pap technique nonetheless is far from perfect and carries a 10-70% false negative rate due to collection and processing errors necessitating that the test be performed annually for optimal performance. Also, in a developing country like India, cytology based screening programs are difficult to organize because of absence of trained manpower, infrastructure, logistics, quality assurance, frequency of screening and costs involved.[4] Cancer of cervix is now thought to be a sexually transmitted disease. Its association with early sexual activity and sexual promiscuity in particular, has been well established. It has been suggested that cervical cancer might be caused by sexual transmission of an infectious agent and HPV

Colposcopy is an integral part of the management of women presenting with abnormal cervical cytology and those with lesions in the lower genital tract indicative of intraepithelial neoplastic disease. Colposcopy as a subjective modality has a sensitivity for the detection of intraepithelial disease in the range of 60-75%. When employed with exfoliative cytology, this sensitivity can be increased to >90%. The sensitivity of a combined Pap and Human Papilloma Virus (HPV) testing strategy is further enhanced by referring all women with Low grade squamous intraepithelial lesion (LSIL) or High grade squamous intraepithelial lesion (HSIL) cytology to colposcopy regardless of HPV result.[5] Cytology and colposcopy are being widely used for this purpose and we are comparing and correlating the findings of pap smear and colposcopy with the gold standard histopathology in a hospital based setting in symptomatic women and suspicious looking cervix. The concept of pre-invasive disease of cervix, which denotes changes that are confined to the cervical epithelial cells, was introduced in 1947. Early detection and treatment of pre invasive disease has the potential to improve the outcome of patients.

In low-resource countries like India, facilities for screening asymptomatic women are not readily available, and cultural attitudes and lack of public education also discourage early diagnosis. Hence, most

patients in developing countries like India present with advanced disease that may have already eroded into the bladder, rectum, pelvic nerves, or bone. Because radiation therapy and palliative care facilities are also usually inadequate, many of these women die as social outcasts, with severe pain and a foul-smelling vaginal discharge. Most of these women have dependent children, so the social devastation caused by this disease can be readily appreciated. Hence, cervical cancer screening plays a vital role in decreasing the disease burden and helps in reducing cancer related morbidity and mortality. Present study is carried out to evaluate colposcopy and cytology in cervical cancer screening

II. Materials And Methods

This study is a prospective observational study. The present study was carried out in Command Hospital AirForce (CHAF), Bangalore in Department of Obstetrics and Gynaecology.100 patients with unhealthy cervix attending the OPDwere selected.Among patients with unhealthy cervix who satisfied the inclusion criteria were selected for the study. Women with the following criteria were included in the study-Age between 20-60 years, patients with abnormal symptoms like profuse white discharge, post coital bleeding, inter menstrual bleeding or postmenopausal bleeding, clinically unhealthy cervix diagnosed by speculum examination like cervical erosion, cervicovaginitis, cervical polyp, condylomas etc. Following patients were excluded from the study women with age > 60 years and < 20 years-women with frank invasive cancer,who underwent total hysterectomy and pregnant women.

Following were used-video colposcope with magnification upto 40X with inbuilt green filter is used. Magnification of 10X was preferred for visualizing the entire cervix and for examining angioarchitecture. Distance of 250mm-300mm is preferred. This allowed easy working and manipulation of instruments without hampering vision. Colposcopy and pap smear was done in unhealthy cervix and sensitivity, specificity, positive predictive value, negative predictive value and accuracy of both the methods were found taking histopathology as gold standard. After taking informed consent the observations from the per speculum examination was recorded and a Pap smear would be obtained if there was no previous pap report. Visual findings were recorded under the heading of unaided visual inspection of cervix on the proforma.

In symptomatic women, the exfoliated cells from the cervix were sampled using the Ayer's spatula which fit into the contour of the ectocervix and endocervix was sampled using an endocervical sampling brush. The material obtained was smeared evenly on a glass slide fixed using fixative containing 50% alcohol and 50% ether. The smears were sent to the cytopathology laboratory in the same hospital. The cervical smears were stained with Papanicolaou technique and then screened and reported according to the Bethesda System. Then colposcopy was performed using video colposcope with an optical zoom up to 40x was used. In all 100 women colposcopy was done according to conventional method. The cervix was visualized under low power 10x to note any abnormal findings. Capillaries and surface blood vessels of the cervix was visualized under low power to note any abnormal findings. Capillaries and surface blood vessels were examined with a green filter.5% glacial acetic acid was gently applied over the cervix for a total period of one minute, to ensure appropriate acetowhite reaction. Transformation zone was defined between the old and new squamocolumnar junctions. Colposcopy was considered unsatisfactory if the new squamocolumnar junction was not visualized completely and endocervical curettage was performed. Examination of each quadrant was done in a clockwise direction. If acetowhite reaction was seen in the transformation zone; then margin, colour, vessels and colposcopy signs were noted. Lugol's iodine was applied and findings documented.Colposcopy guided biopsies were taken with punch biopsy forceps from the site with suspicion and transferred to a vial containing 10% formaldehyde and sent for histopathological examination. Unsatisfactory colposcopy was recorded separately. Pap smear and colposcopy were correlated with histopathology obtained from colposcopic directed biopsies and further management was decided.

III. Results

Age Distribution(Table 1)

Age	No. of cases	CIN cases percentage (%)	
30 – 40	42	1	5.5
41- 50	48	15	83.3
51 – 60	10	2	11.1

Clinical appearance of cervix (Table 2)

Clinical appearance of	Total cases	CIN Cases No. (%)
Cervix		
Erosion of cervix	45	10 (55.5)
Hypertrophy	19	4 (22.2)
Hypertrophy + Erosion	22	3 (16.6)
Cervical polyp	5	0

Leukoplakia	4	0
Hyperemia	5	1 (5.5)

Acetic acid applications (Table 3)

Acetic area within transformation zone	Total cases	CIN (%)
Flat AW areas with geographic margins and mild AW areas.	26	16 (88.8%)
Dense, opaque AW area with sharp margin with punctate /mosaic	02	02(11.2%)
TOTAL	28	18

Table 1 shows that among 100 women, 42% were between 30-40 years, 48% were between 41- 50 and 10% between 51-60 years. The incidence of CIN-was 5.5% in 30-40years, 83.3% in 41-50years age group and 11.1% in the age group of 51-60. Incidence of CIN was found to increase as age increases. In present study incidence of CIN was found to be high in 41-50 age group. Table 2 shows that, erosion was found in 45%, hypertrophy with erosion in 22%, hypertrophy in 19%, polyp was found in 5%, leukoplakia in 4% of cases and hyperemia in 5% of cases. Among women with erosion cervix 55.5 % had CIN. Among those with congestion 5.5% had CIN. Among those with hypertrophy 22.2% were found to have CIN, and in those who had hypertrophy with erosion 16.6% had CIN. All polyps were benign**.**

Colposcopic appearance of cervix (Table 4)

Appearance	No. of cases
Erosion of cervix	67
Polyp	5
Leukoplakia	2
AW areas	28
Punctate pattern	2
Mosaic pattern	2
Atypical vessels	-

HPE findings (Table 5)

HPE	NO of cases
Chronic cervicitis	34
Acute on chronic cervicitis	18
Papillary endocervicitis	09
Polyp	05
CIN-I	15
CIN-II	01
CIN-III	02
Microglandular hyperplasia without atypia	08
Koilocytic changes	06
Adenocarcinoma cervix	02

Comparison of Pap smear, colposcopy and HPE with unhealthy cervix (Table 6)

Indications	Cases	Pap Smear						Colposcopy			Histology				
		P1	P2	P3	P4	P5	P6	C1	C2	C3	H1	H2	H3	H4	H5
Cervical Erosion	42	26	08	01	04	03		31	11		30	08	01	02	01
Cervical Hypertrophy	19	12	05		01	01		12	02	01	17	02			
Nabothian Cyst	03	01	01		01			02	01		01	02			
Hypertrophy + Erosion	22	12	05		02	01	02	15	06	01	19	02			01
Polyp	05	03	02					05			05	02			
Leukoplakia	04	03	01					03	01		03				
Hyperemia	05	03	01		01			04	01		05	01			03
Total	100	43	23	01	09	05	02	72	26	02	80	15	01	02	02

P1-NILM, P2-ASCUS, P3-ASC-H, P4-LSIL, P5-HSIL, P6-Invasive Carcinoma
C1-Normal, C2-Mild Acetowhite Areas, C3- Dense Acetowhite Area with Punctate and Mosaic

PatterH1-Normal, H2-CIN 1, H3-CIN 2, H4-CIN 3, H5-Adenocarcinom

Comparison of pap smear, colposcopy and HPE findings (Table 7)

Pap Smear		Colposcopy			HPE				
	Cases	C1	C2	C3	H1	H2	H3	H4	H5
NILM	60	35	15		59	01			
ASCUS	23	18	05		16	06	01		
HSIL	05	03	01	01		03		01	01
LSIL	09	05	04		04	05			
ASC(H)	01			01				01	
AGC	02	01			01				01
Total	100	72	26		80	15	01	02	02

C1-normal, c2-mild acetowhite areas, c3- dense acetowhite areawith punctate and mosaic pattern
H1-normal, h2-CIN 1, h3-CIN 2, h4-CIN 3, h5-adenocarcinoma

Comparison of Pap smear and colposcopy (Table 8)

PAPSMEAR	PAP SMEAR NO	COLPOSCOPY		
		C1	C2	C3
NILM	60	49	11	
ASCUS	23	18	05	
LSIL	09	03	06	
HSIL	05	02	02	01
ASCUS –H	01	-	01	
AGC	02	-	01	01

C1-Normal, C2-Mild Acetowhite Areas, C3- Dense Acetowhite Areawith Punctate and Mosaic Pattern

Table 3 shows that flat AW areas with sharp margins within the transformation zone indicated immature metaplasia or low grade CIN. Among those with flat AW areas, 88.8% had CIN. Among those with dense opaque AW area, 11.1% had CINII and CINIII. Most of the patients examined had findings of mild AW areas. According to Table 4, Among the 100 cases studied, 28% were diagnosed as colposcopically abnormal. Among the abnormal cases, AW areas were diagnosed in 28%.punctate pattern of vessels was seen in 2%of women and mosaic pattern of vessels was diagnosed in 2% of women. Erosion cervix in 67%, and polyps were diagnosed in 5%, leukoplakia was found in 2% of cases. According to Table 5, 61 % had cervicitis, 15% had CIN I, 1% had CINII and 2%had CINIII and 02 % had adenocarcinoma

Comparison of Pap smear with HPE reports (Table 9)

Pap smear report	No. of patients	Normal biopsy report	CIN-I	CIN-II	CIN-III	Adenocarcinoma

NILM	60	59	01	-		
LSIL	09	03	O6	-		
HSIL	05	-	03		01	01
ASCUS-U	23	17	05	01		
ASCUS-H	01	-	-		01	
AGC	02	01	-			01

True positive = 9 False positive = 3 True Negative = 80 False Negative = 8

Sensitivity and Specificity of pap smear (Table 10)

Sl no	Parameter	Percentage
01	Sensitivity	52.94%
02	Specificity	96.38%
03	Positive predictive value	75%
04	Negative predictive value	90.9%
05	Diagnostic accuracy	89%

Sensitivity and specificity of colposcopy (Table 11)

Colposcopy	HPE		Total
	Positiv3	Negative	
Positive-28	TP-20	FP-08	28
Negative-72	FN-1	TN-71	72
Total	17	83	100

Sensitivity	95.23%
Specificity	89.87%
Positive Predictive Value	71.42%
Negative Predictive Value	98.7%
Accuracy	91%

IV. Discussion

Cervical cancer is the second most frequent cancer worldwide, in women after breast carcinoma. However, invasive cancer of the cervix was consider to be a preventable condition as it associated with a long pre invasive stage (CIN) making it amenable to screening and treatment. Cervical cancer has an uneven geographic distribution with majority of cases being in the developing countries. Declining trends in the developed countries over the last few decades are attributed to the implementation of organized screening programmes by Pap smear. Colposcopy as a clinical method has been of proven accuracy in evaluating patients with abnormal cervical cytology. But its value as a screening tool has long been disputed. As effective cytological screening in our country in still not successful, there is a necessity to find other ways to deal with this problem. In the present study, screening was done in 100 women with abnormal cervix and abnormal symptoms like excessive white discharge post coital bleeding, post-menopausal bleeding etc., with colposcopy and its result were correlated with Pap smear taking histopathology finding as gold standard to determine the sensitivity and specificity of these methods in detecting CIN.

Regarding age distribution, Kushtagi and Fernands, in their study showed the prevalence of CIN was higher in women over 30 year.[6] Vaidhya et al showed in his study that CIN was more prevalent in the age group of >35 years.[7] Shalini et al showed the mean age patients with cancer cervix were 41 vs 32 in patients

with benign pathology in cervix.[8] In our study, high incidence of CIN was found among the age group of 40-50 years with 75% of cases with mean age 42.20yrs. The results are similar to the other studies. Although, many authors observed an inverse relationship between the distribution of cervical cancer and the educational status of women. CIN is more prevalent among the illiterates. This was attributed to lack of awareness of symptoms and failure to seek medical care. Present study did not show any correlation between the educational status and preinvasive lesions of cervix. In our study most of the subjects were educated with only 6% of the subjects were illiterates, accounting to 1% of CIN cases. Socio-economic status has always been playing an epidemiological role in genesis of dysplasia. Poor socio-economic status has linear relationship with increasing risk of cervical cancer. In our study, patients belong to fixed income group. However, many Indian studies have reported that women from lower socioeconomic strata had higher incidence of cervical cancer. [9, 10]

Many authors have discussed a strong influence of early coitus and multiparity on the risk of cervical cancer as in the present study.[11,12,13] Similar study by Shalini et al showed the mean parity was 4.2 in patients with invasive cancer.[8] Kushtagi and Fernandez showed the prevalence of CIN was significantly higher in parity of more than 2.[6] Vaidya showed more positive cases of CIN were found with parity more than 4.[7]This might be attributed to hormonal and nutritional changes that occur in pregnancy, immunosuppression during pregnancy, and cervical trauma during vaginal delivery (Becker et al and Adadevoh et al).[14] Regarding party, our study showed, increased incidence of CIN among Para 2 women with 72.2%. In the study, most of the patients about 69% were Para 2. Studies have shown increased incidences of cervical cancer in multiparous women. Duration of marriage and duration of exposure to sexual intercourse increases the risk of cervical cancer Kushtagi et al had demonstrated the Severity of underlying CIN increased with increase in the duration of marital life and hence the increase in the duration of sexual intercourse. [6] Increasing number of sexual partners had the effect on increasing the risk of developing CIN and invasive disease. Sex with high risk males was also another risk factor for the development of CIN. In our study, the incidence of CIN was 83.3% in women married for >20 years, and 25% among women who were married for > 20 years. The relationship between oral contraceptives and development of CIN had been investigated by IARC – International agency for Research in Cancer and they concluded that the use of OCP increased the risk of CIN up to 4 fold after 5 or more years among the HPV DNA positive women. Regarding contraception in our study, most of the women had permanent sterilization or using no contraception or natural methods. Barrier method of contraception was used in 4% found that none of the women who practices barrier contraception had CIN. Out of 58% of women who had undergone sterilization permanently the incidence of CIN was 50%.

Post coital bleeding was found in 13% of cases. Among them CIN was found in 11.1%. Shalini R, Amitha S, in their study showed the relationship of post coital bleeding and CIN. In their study, among the women who had post coital bleeding, 85.5% had benign findings, 5.6% had HPV and CIN I, 3.6% had CIN II and III and 55% had invasive cancer. There was no correlation between the duration of bleeding and pathology. Among those with intermenstrual bleeding, 33.3 % had CIN. Among those with post-menopausal bleeding 11.1% had CIN. Regarding sensitivity and specificity of Pap smear Shalini R et al found Pap smear more specific with 90% specificity and less sensitive with 56% sensitivity. [8] Basu PS and Sankaranarayanan in their study found Pap smear to be 29.5% Sensitive and 92.3% specific. [15] In the present study, we found Pap smear to be more specific with specificity of 95.25% and less sensitive with 52.9% sensitivity which is similar to other studies.

This shows that Pap smear is less sensitive as a screening method and in cases of clinically unhealthy cervix even with normal cytology colposcopy to be used for confirmation. This data suggested that with colposcopy as a screened tool, the rate of false negative cytology could be significantly reduced. Colposcopy enhanced cervical screening particularly in women with otherwise negative smears, Correlation between cytology and HPE was poor as far as mild dysplasia were concerned. But the correlation was good for moderate and severe dysplastic lesions.

Colposcopy as a screening modality has been studied by many authors. Sukhpreet L Singh et al in his study found sensitivity and specificity of colposcopy to be 95% and 63.5. [16] Olaniyan B did a meta-analysis by reviewing 8 longitudinal studies and found sensitivity and specificity ranging from 87-99% and 26-87%.[17] Massad et al concluded colposcopy is more sensitive with 89% sensitivity and 52% specific.[18] In our study, we found the similar results with sensitivity and specificity of 95.2% and 89.8%. This showed a high sensitivity and a low specificity when compared to Pap smear. Low specificity when compares to Pap smear was due to the high incidence of unsuspected AW epithelium which might be to inflammation, immature metaplasia, and latent HPV infections. Out of 28 cases which showed AW areas 20 were confirmed by biopsy.

Olaniyan et al, in his meta-analysis compared the correlation of colposcopy impression with biopsy results. Colposcopy accuracy was found to be 89% which agreed exactly with histology in 61% of cases.[17] Massad et al reported an accuracy of 80%.[18] In the present study, the accuracy colposcopic impression was found to be 91%.

V. Conclusions

Pap smear had a sensivity of 52.94% and a specificity of 96.38% with positive predictive value of 78% and negative predictive value of 90.9% and diagnostic accuracy of 89% while the colposcopy had sensitivity of 95.23 % and a specificity of 89.87% with positive predictive value of 71.42 % and negative predictive value of 98.7% and diagnostic accuracy of 91%. PAP smear is less sensitive and more specific compared to colposcopy. Both Pap smear and colposcopy are complementary to each other. Hence, Papsmear, colposcopy and guided biopsy in single sitting is the best approach for the early detection and diagnosis of carcinoma cervix.

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