Screening for Carcinoma Cervix by Comparing Pap Smear Cytology, Histopathology with Colposcopy in Unhealthy Cervix
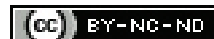
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ABSTRACT

Introduction: Cervical cancer is one of the most frequent genital tract cancers and accounts for 80% of all female cancers worldwide. Annually, the incidence is about five lacs and 2,80,000 people die due to carcinoma cervix yearly. In India, 1,26,000 new cases are detected and 71,000 deaths occur annually. Cervical cancer is a preventable condition, since it is associated with prolonged preinvasive stage, so that early screening and appropriate treatment can be undertaken to prevent the progression into invasive stage.

Aim: To compare Papanicolaou (Pap) smear cytology, colposcopy and colposcopy guided biopsy (histopathology) in detecting premalignant and malignant lesions of the cervix.

Materials and Methods: A cross-sectional study was carried out in Department of Obstetrics and Gynaecology at RL Jalappa Hospital and Research Centre, Kolar, Karnataka, India. The study period was from October 2018 to June 2020 and 90 study subjects were included in the study. All the study subjects enrolled were subjected to Papanicolaou (Pap) smear, colposcopy and colposcopy directed biopsy. The data was statistically analysed for sensitivity, specificity, positive predictive value, negative predictive value and accuracy of pap smear and colposcopy, with considering colposcopy directed biopsy as the gold standard for diagnosis.

Results: Maximum number of women was found in the age group of more than 50 years (44.4%), mean age was 52±11 years. Majority of the women were multipara accounting for 95.6%. Pap smear had a sensitivity and specificity of 69.2% and 88.2%, respectively. The colposcopy had sensitivity of 97.37% specificity of 88.46 as Pap smear.

Conclusion: Colposcopy has a good association with Pap smear and histopathology in diagnosis of premalignant and malignant lesion in unhealthy cervix. Hence, its satisfactory diagnostic efficacy makes it a realiable for diagnosis of malignant and pre malignant lesion.

Keywords: Atypical squamous cell carcinoma, Cervical malignancy, Papanicolaou smear

INTRODUCTION

Cervical cancer is the most common cancer among Indian women and early detection of it in women with unhealthy cervix is very important to reduce the morbidity and mortality [1]. The visual evaluation of unhealthy cervix is unreliable and many premalignant lesions are missed and considered as straightforward cases of erosion of cervix because of inflammation.

Uterine and cervical cancer is a stern health issue in India [2]. Indian sub-continent accounts for one fifth of the world's burden of cervical cancer. Invasive cancer of cervix is preventable since it has a long preinvasive state, so that prompt cervical cytology screening and treatment can be undertaken to prevent the progression into malignancy [3]. The direct visualisation of the cervix with simple sampling technique has reduced the requirement of extensive investigations on cervical lesions. The present evidence shows that malignancy of cervix develops from dysplasia. Hence, cervical screening by cytology and colposcopy can considerably reduce the rate of malignancy [3].

Papanicolaou (Pap) smear is most common method used for screening of cervical cancer. Its merits include simplicity of the procedure, low cost, less time consuming, early diagnosis and good specificity [4]. However, there are certain demerits like a low sensitivity rate of 51 percent and a false negative rate of 49 percent [4].

Colposcopy is a simple out-patient method of visualising the female reproductive and genital tract under bright radiance using stereoscopic vision to identify abnormal lesions. It is considered to be superior to cytology. It helps in making accurate indications for cervical biopsy, by pin-pointing sites for biopsy. It helps in avoiding unnecessary diagnostic procedure for simple lesions caused due to inflammation and also helps us in making accurate diagnosis. Biopsy of the cervical lesions is considered to be the gold standard method to arrive at the ultimate diagnosis [4].

Colposcopy aids in identifying the exact lesions so that the biopsy can be taken which is considered as the gold standard in diagnosis of malignant lesions [5]. Hence, this study was conducted with the aim to perform cytology, histopathology and colposcopy in patients with unhealthy cervix and compare these tests to determine an early diagnosis of cervical cancer.

MATERIALS AND METHODS

This cross-sectional study was conducted on patients who attended the Gynaecological Outpatient Department at RL Jalappa Hospital and Research Centre, Kolar, Karnataka, India. The study period was from October 2018 to June 2020. Institutional Ethical Committee clearance was obtained before commencement of study. Participants were told about the procedure in brief and written informed consent was taken. Women with unhealthy cervix which is characterised by abnormal growth, ulcer/erosion, vasculature on inspection were included [5].

Inclusion criteria:

1. All sexually active females age >18 years to 55 years.

2. Patients with unhealthy cervix such as cervical erosion, cervical polyp, cervicovaginits, bleeds on touch.

3. Women with presenting complaints such as white discharge per vaginal, intermenstrual (n-10) and postcoital bleeding.

Exclusion criteria:

1. Pregnant women as it is associated with increased false positive results because of hyperdynamic state.

2. Active bleeding as it obscures the cytological examination.

Sample size calculation: The sample size of 90 was estimated based on a previous study [6] conducted with sensitivity of 94.7%, precision of 2% with confidence interval of 95%.

Presenting complaint, obstetric history, menstrual history, any significant medical history, family history was taken. The patient was examined in dorsal position, retracting the anterior and posterior vaginal wall using the Cusco's speculum and the cervix was examined for any unhealthy features.

Pap Smear

After inspection of the uterine cervix, Pap smear was taken with Ayre's spatula from the Squamo Columnar Junction (SCJ) by rotating 360 degrees. The obtained specimen was spread on a glass slide and fixed with 95% of ethyl alcohol and smears were analysed by the pathologist as per Bethesda System of Classification [7].

Colposcopy

Colposcopy was done in women with unhealthy cervix irrespective of pap results. Using normal saline, green filter and acetic acid colposcopy was performed. Colposcopy diagnosis was made based on the findings recorded using Modified Reid Colposcopy Index (RCI) [8]. The three objective categories were based on four colposcopy signs which are colour, margin (including surface contour), vascular pattern and iodine response. Each category was offered scores of 0 to 2 and sum of all the categories was taken for final grading of Cervical Intraepithelial Neoplasia (CIN). The grading is as follows:

0-2:- Likely to be CIN 1

3-4:- Overlapping lesion: likely to be CIN 1 or CIN 2

5-8:- Likely to be CIN 2-3

Colposcopy-guided biopsy: Under colposcopy guidance, biopsy was taken from the abnormal area using cervical punch biopsy forceps and the biopsy results were categorised as:

1. Cervicitis/metaplasia

2. CIN-1 (mild dysplasia/correlating with Low Grade Squamous Intraepithelial Lesion (LSIL)

3. CIN-2/3 (moderate to severe dysplasia/correlating with High Grade Squamous Intraepithelial Lesion (HSIL)

4. Squamous cell carcinoma

STATISTICAL ANALYSIS

Data were entered in Microsoft Excel and analysed in Statistical Package for the Social Sciences (SPSS) version 21.0. Descriptive statistics were represented with frequencies and percentages, sensitivity and specificity were calculated. The p-value <0.05 was considered as statistically significant. Kappa test was used to calculate the diagnostic accuracy of Pap smear and colposcopy.

RESULTS

Maximum number of women was found in the age group of more than 50 years (44.4%), mean age was 52±11 years. Majority of the women were multipara accounting for 95.6% [Table/Fig-1].

The most common symptom in the study participants was white discharge per vagina (67.8%). On clinical examination erosion was present in majority (55) of the patients [Table/Fig-2].

Most common finding on pap smear was inflammation (27.8%) [Table/Fig-3]. Most common finding on colposcopy was inflammation/squamous metaplasia/erosions (40%) while only 5 subjects had a normal colposcopy [Table/Fig-4].

Variables	N (%)
Age (years)	
20-29	11 (12.2)
30-39	10 (11.1)
40-49	29 (32.2)
>50	40 (44.4)
Parity	
Nullipara	1 (1.1)
Primipara	3 (3.3)
Multipara	86 (95.6)

[Table/Fig-1]: Distribution of women according to age and parity.

Symptoms	N (%)
Intermenstrual bleeding	10 (11.1)
Postcoital bleeding	19 (21.1)
White discharge per vaginum	61 (67.8)
Total	90 (100)
Per speculum/per vaginal finding	
Erosion	55 (61.1)
Hyperemia	40 (44.4)
Bleeds on touch	10 (11.1)

[Table/Fig-2]: Distribution of women based on symptoms and per speculum findings.

Pap smear results	N (%)
Normal	24 (26.6)
ASCUS	8 (8.9)
Inflammatory	25 (27.8)
LSIL	13(14.4)
HSIL	15 (16.7)
Malignancy	5 (5.6)
Total	90 (100)

[Table/Fig-3]: Pap smear findings.
ASCUS: Atypical squamous cells of undetermined significance; LSIL: Low grade squamous Intraepithelial lesion; HSIL: High grade squamous Intraepithelial lesion

Colposcopy results findings	N (%)
Normal	5 (5.6)
Inflammation/squamous metaplasia/erosion/Transformation zone seen/hyperaemia	36 (40)
Hazy/fine acetowhite area/fine punctation or mosaicism (LSIL)	21 (23.3)
Dense acetowhite area/coarse punctation or mosaicism (HSIL)	11 (12.2)
Unsatisfactory	6 (6.7)
Malignancy (intense acetowhite area, coarse irregular punctation	11 (12.2)
Total	90 (100)

[Table/Fig-4]: Colposcopy findings.

Most common biopsy finding was metaplasia which accounted for 56.7% [Table/Fig-5].

The significant finding that was noted was malignancy, which was diagnosed only in five cases on Pap smear but it was 12 on biopsy [Table/Fig-6].

Colposcopy-guided biopsy results	N (%)
Cervicitis/Metaplasia	51 (56.7)
Mild Dysplasia (LSIL)	15 (16.7)
Moderate Dysplasia/Severe Dysplasia (HSIL)	12 (13.3)
Squamous cell carcinoma	12 (13.3)
Total	90 (100)

[Table/Fig-5]: Colposcopy-guided biopsy findings.

Thirty three cases out of 90 study participants were positive on pap smear; while it was 39 on biopsy. Pap smear was positive in 27 out

Pap smear	Biopsy				Total
	Cervicitis/ Metaplasia	Mild dysplasia/ LSIL	Moderate dysplasia/Severe dysplasia/HSIL	Malignancy	
Normal	24	0	0	0	24
ASCUS	5	2	1	0	8
Inflammatory	16	8	0	1	25
LSIL	4	4	2	3	13
HSIL	2	1	9	3	15
Malignancy	0	0	0	5	5
Total	51	15	12	12	90

[Table/Fig-6]: Comparison between Pap smear and Colposcopy-guided biopsy.
ASCUS: Atypical squamous cells of undetermined significance; LSIL: Low grade squamous Intraepithelial lesion; HSIL: High grade squamous Intraepithelial lesion

of 39 biopsy proven positive cases. Agreement between cytology and biopsy was poor with a p-value of <0.001 [Table/Fig-7].

Comparison between colposcopy and biopsy shown in [Table/Fig-8]. Colposcopy was unsatisfactory in six cases, one case of moderate dysplasia Case underreported as metaplasia on colposcopy. Five cases of cervicitis were over reported as Low grade squamous intraepithelial lesion (LSIL)/High grade squamous intraepithelial lesion (HSIL) on colposcopy.

Pap smear	Biopsy		Total
	Positive	Negative	
	n (%)	n (%)	n (%)
Positive	27 (69.2%)	6 (11.8%)	33 (35.0%)
Negative	12 (30.8%)	45 (88.2%)	57 (55.5%)
Total	39 (100.0%)	51 (100.0%)	90 (100.0%)

[Table/Fig-7]: Diagnostic efficacy of Pap smear.
Kappa value=0.62; p-value <0.001

Colposcopy	Biopsy				Total
	Cervicitis/ Metaplasia	Mild dysplasia	Moderate dysplasia/ Severe dysplasia	Malignancy	
Normal	5	0	0	0	5
Inflammation/squamous metaplasia/erosion/ transformation zone seen/hyperaemia	35	0	1	0	36
Hazy/fine acetowhite area/fine punctation or mosaicism (LSIL)	4	13	4	0	21
Dense acetowhite area/ coarse punctation or mosaicisim (HSIL)	1	2	7	1	11
Unsatisfactory	6	0	0	0	6
Malignancy (intense acetowhite area, coarse irregular punctation	0	0	0	11	11
Total	51	15	12	12	90

[Table/Fig-8]: Comparison between colposcopy and biopsy.

Total 43 out of 90 women were positive on colposcopy; while it was 39 on biopsy. Colposcopy was positive in 38 out of 39 biopsy proven positive cases. Agreement between colposcopy and biopsy was good and the p-value was <0.001 which was statistically significant [Table/Fig-9].

Sensitivity of Pap smear was 69.2%, specificity was 88.23% and accuracy was 81.71%. Sensitivity of colposcopy 97.37%, specificity is 88.46% and accuracy is 92.22% [Table/Fig-10].

The combined sensitivity of Pap smear and colposcopy was 97.37% and specificity was 88.46% and accuracy was 92.22%

which is more when compared to Pap smear, when used alone as a screening test [Table/Fig-11].

Colposcopy	Biopsy		Total
	Positive	Negative	
	n (%)	n (%)	n (%)
Positive	38 (97.4%)	5 (11.5%)	43 (47.7%)
Negative	1 (2.6%)	46 (88.5%)	47 (52.3%)
Total	39 (100.0%)	51 (100.0%)	90 (100.0%)

[Table/Fig-9]: Diagnostic efficacy of colposcopy.
Kappa value=0.84; p-value <0.001

Statistic	Pap smear % (95% CI)	Colposcopy % (95% CI)
Sensitivity	69.2 (56.74-87.51)	97.37 (86.19-99.93)
Specificity	88.23 (74.26-95.17)	88.46 (76.56- 95.65)
Positive predictive value	81.25 (66.69-90.37)	82.05 (74.36-92.91)
Negative predictive value	82.00 (71.96-88.99)	97.87 (86.90-99.69)
Accuracy	81.71 (71.63-89.38)	92.22 (84.63-96.82)

[Table/Fig-10]: Sensitivity and specificity of Pap smear and colposcopy.

Statistic	Value	95% confidence interval
Sensitivity	97.37%	86.19% to 99.93%
Specificity	88.46%	76.56% to 95.65%
Positive predictive value	86.05%	74.36% to 92.91%
Negative predictive value	97.87%	86.90% to 99.69%
Accuracy	92.22%	84.63% to 96.82%

[Table/Fig-11]: Sensitivity and specificity of Pap and colposcopy.

A total of 43 out of 90 study participants were positive on colposcopy and 33 on Pap smear. Pap smear was positive in 28 out of 44 positive colposcopies. Sixteen study participants were under reported negative which was positive on colposcopy [Table/Fig-12].

Colposcopy	Pap						Total
	Normal	ASCUS	Inflam-matory	LSIL	HSIL	Malig-nancy	
Normal	4	0	0	1	0	0	5
Inflammation/ Squamous Metaplasia/ Erosion/ Transformation zone seen/ Hyperaemia	16	5	12	2	1	0	36
Hazy/Fine Acetowhite Area/ Fine Punctation or Mosaicism	1	2	8	6	4	0	21
Dense acetowhite area/ Coarse punctation or mosaicisim	0	1	2	1	7	0	11
Sunsatisfactory	3	0	2	0	1	0	6
Malignancy (Intense acetowhite area, coarse irregular punctation	0	0	1	3	2	5	11
Total	24	8	25	13	15	5	90

[Table/Fig-12]: Comparison between colposcopy and Pap smear.
ASCUS: Atypical squamous cells of undetermined significance; LSIL: Low grade squamous Intraepithelial lesion; HSIL: High grade squamous Intraepithelial lesion

The sensitivity of Pap smear in relation to colposcopy was only 65.50% and specificity was 89.10%. The positive predictive value was 83.38% and the negative predictive value was 73.0% with an accuracy rate of 78.05% [Table/Fig-13].

Statistic	Value	95% confidence interval
Sensitivity	65.50%	50.87% to 81.43%
Specificity	89.10%	74.37% to 96.02%
Positive predictive Value	83.38%	69.76% to 92.67%
Negative predictive Value	73.00%	64.24% to 81.85%
Accuracy	78.05%	67.54% to 86.44%

[Table/Fig-13]: Sensitivty and specificity of Pap in relation to colposcopy.

DISCUSSION

World wide, cervical carcinoma is the second most common type of cancer. The high incidence of cervical carcinoma is mainly due to lack of awareness of the disease amongst the people illiteracy due and low socio-economic status [9]. The blessing in disguise for this slow progressive disease lies in the fact that it has got a long preinvasive period and if detected early in this phase, will bring down the incidence of CIN and frank cervical carcinoma. Pap smear has high specificity when compared to sensitivity whereas colposcopy has high sensitivity and specificity hence Pap smear along with colposcopy can detect the lesions early in its preinvasive phase and can prevent deadly consequences [9]. In the present study, it was found that the combination of Pap smear along with colposcopy increased the likelihood of detecting premalignant lesion in an unhealthy cervix.

Olaniyan OB did a meta-analysis of eight longitudinal studies and compared the correlation of colposcopy impression with biopsy results [10]. Colposcopy accuracy was found to be 89% which agreed exactly with histology in 61% of cases. In the present study, the accuracy of colposcopy impression was found to be 92.2% in relation with biopsy.

Joshi C et al., showed that the CIN I was 28%, CIN II 11%, CIN III 4%. Authors emphasized the use of all 3 methods Pap cytology (conventional method), colposcopy, and histology is complementary to each other and helps to reduce false negative cases [11]. Gupta P et al., concluded that the accuracy of cytology when compared to colposcopy was 81.82%, in the present study it is 78.05% [12]. The accuracy of colpo-histopathology was 83.6% in the study conducted by Dorji N et al., which is similar to the present study (92.2%) [13].

In a study conducted by Poudel A and Dahal P, 54 cases were evaluated [14]. In a total of 54 cases of Pap smears, 30 (55.55%) were concordant, while discrepancies occurred in 24 (44.44%) cases with cervical biopsy. So, the study revealed a good correlation between cervical cytology and cervical biopsy, which is contrary to the present study.

Sawant D et al., concluded that cytology and colposcopy combined can become a better method for screening in perspective of high sensitivity, specificity and positive predictive value, which is similar to the present study [15]. In the present study, most cases of CIN were found among the age group of above 50 years (44.4%) with mean age of 52±11 years. Kushtagi P and Fernandes P showed the overall prevalence of CIN was more in women over 30 years [16]. Similarly, Vaidya A in his study showed that prevalence of CIN was more in the age group of more than 35 years [17]. All these studies indicate that premalignant and malignant lesion of the cervix is most commonly seen in elderly age group.

In the present study, increased incidence of CIN was noted in multiparous women (95.6%). A study which was similar to present study done by Shalini R et al., showed the mean parity was 4 in patients with invasive carcinoma cervix [18]. Kushtagi P and Fernandez P in their study concluded that the prevalence of CIN was higher in multiparous women [16]. In a study done by Vaidya A showed more positive cases of CIN were found in women with parity more than four [17]. This might be attributed to the nutritional and hormonal changes that occur in pregnancy, immune-suppression during pregnancy and cervical trauma during vaginal delivery. Majority of women (67.8%) complained of excessive white vaginal discharge. Vaidya A concluded that white discharge accounted for 24% of cases [17]. He postulated that excessive vaginal discharge played a significant role for the development of CIN. In the present study postcoital bleeding was found in 21.1% of cases. Shalini R et al., showed the relationship of postcoital bleeding and CIN [18].

Limitation(s)

There may be observer bias in reading of colposcopy and sample size is less. It is a single centre study so the findings of the study cannot be generalised.

CONCLUSION(S)

Colposcopy is unquestionably more reliable than Pap smear because of its sensitivity and accuracy. Best result in early detection of preinvasive carcinomas could be obtained by combined use of cytology and colposcopy directed biopsy. By combining Pap smear with colposcopy, one can make cervical screening programme an effective programme by increasing the sensitivity and reducing the morbidity and mortality rate.

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