

Analytical study of symptoms and various screening modalities in cervical cancer

Dr Pratyaksha Raina¹, Dr Pooja Sharma^{2*}, Dr Rohini Jaggi³

¹Senior Resident, Department of Obstetrics and Gynaecology, SMGS Hospital, Jammu

²Lecturer, Department of Obstetrics and Gynaecology, SMGS Hospital, Jammu.

³Senior Resident, Department of Obstetrics and Gynaecology, SMGS Hospital, Jammu

*pooja.polar1@gmail.com

ABSTRACT

INTRODUCTION: Cervical malignancy is a common, preventable, and curable cause of morbidity and mortality. Cervical cancer is preceded by a long phase of premalignant cytological changes that takes over a period of 15-20 years for the invasive cancer to develop. Thus, cervical cancer can be prevented, if cellular changes are detected and treated at an early stage. Lack of resources, lack of awareness, lack of effective screening programs and poorly organized health system seem to be the reasons for higher prevalence of cervical cancer in India & other developing countries.

AIM: To evaluate symptoms and to Compare Pap smear & Colposcopy with Cervical Biopsy Histopathology in evaluation of women with abnormal cervical cytology.

OBJECTIVES: To screen symptomatic women and asymptomatic women with unhealthy cervix with Pap smear. To perform Colposcopic evaluation of the cervix for women with abnormal cytology and have Colposcopic directed biopsy. To compare various screening modalities used.

METHODOLOGY: All patients with inclusion criteria in OBG Department of Teerthanker Mahaveer Medical College & Research Center during period of January 2017 to June 2018. After taking thorough history, they were subjected to different screening methods.

RESULTS: The commonest presenting symptom was vaginal discharge (79% of the patients). The sensitivity of PAP smear is 44.8% and the specificity is 92.9%. The Positive Predictive Value of PAP Smear is 72.2% and the Negative Predictive Value is 80.4%. The Accuracy of PAP Smear is 79%. While the Sensitivity of Colposcopy is 86.2% and the Specificity is 81.6%. The positive predictive value is 65.7% and the negative predictive value is 93.5%. The Accuracy of Colposcopy is 83%.

CONCLUSION: Colposcopy with directed biopsy should be the standard of evaluation and management of symptomatic patients with unhealthy cervix, described as the 'gold standard' for the diagnosis of Precancerous cervical lesions. The sensitivity of Pap smear was poor but it had better specificity. Hence it may be better to utilize both tests as they complement each other in screening of precancerous lesions.

Keywords: colposcopy; cervical cancer; pap smear

Introduction

Cervical cancer is the fourth most common malignancy amongst women in the world and is the commonest amongst Indian women. There were an estimated 528,000 new cases of cervical cancer and 266,000 deaths in 2012⁽¹⁾. There are 570,000 new cases in 2018 representing 6.6% of all female cancers. Approximately 90% of deaths from cervical cancer occurred in low- and middle-income countries⁽²⁾. In fact, almost 90% of cervical deaths in the world occur in developing countries, with India accounting for one quarter of the total cases.⁽³⁾ Women living with late stage cervical cancer may experience irregular bleeding, back pain, pelvic pain, fatigue,

leg swelling, loss of appetite, and weight loss^(4,5). Scarcity of resources, lack of awareness, lack of effective screening programs and poorly organized health system seem to be the reasons for higher prevalence of cervical cancer in India & other developing countries.

Cervical malignancy is a common, preventable, and curable cause of morbidity and mortality. Cervical cancer is preceded by a long phase of premalignant cytological changes that takes over a period of 15-20 years for the invasive cancer to develop. Thus, cervical cancer can be prevented, if cellular changes are detected and treated at an early stage⁶. The easy accessibility of the cervix for clinical examination on routine basis in addition with cytology & offering VIA, VILI and tissue sampling procedure if required, have led to extensive screening programs for early detection and confirmation of the carcinoma cervix. Several screening modalities are now available for early detection of cervical cancer and its precursors which differ with regard to their test characteristics, feasibility and economic considerations.⁽⁷⁾

Aim

To evaluate symptoms and to Compare Pap smear & Colposcopy with Cervical Biopsy Histopathology in evaluation of women with abnormal cervical cytology.

Objectives

- To screen symptomatic women and asymptomatic women with unhealthy cervix with Pap smear.
- To perform Colposcopic evaluation of the cervix for women with abnormal cytology.
- To obtain Colposcopic directed biopsy.
- To compare Pap smear findings with cervical biopsy histopathology findings.
- To compare Colposcopic findings (Modified Reid's score) with cervical biopsy histopathology.

Materials and methods

Source of data: All patients with inclusion criteria in OBG Department of Teerthanker Mahaveer Medical College & Research Center during period of January 2017 to June 2018.

Inclusion criteria

- Women with age 21 – 65 years who attended gynecology OPD and complaints of post coital vaginal bleeding, discharge per vagina, inter menstrual bleeding, low backache.
- Women with unhealthy cervix on routine per-speculum examination like cervical erosion, hypertrophied cervix & abnormal growth and/or ulcer.

Exclusion criteria

- Pregnancy

- Post hysterectomy women

Procedure: A detailed history was taken including demographic data like age, socioeconomic status, education, parity, Loss of appetite and weight, age at marriage, age of first intercourse, multiple sexual partners, STD's, immunosuppression, COC use & complaints like intermenstrual / post coital /postmenopausal bleeding, discharge or pain abdomen. Information was noted on Proforma & Patients were subjected to the following tests Complete blood count, Random Blood Sugar, Urine routine & microscopy. PAP smear was performed by Conventional method. Ayre's Spatula was rotated through 360 degrees maintaining contact with ectocervix. Sample were smeared evenly on the slide and fixed immediately. Both sides of spatula were smeared. The cytological interpretation of the smears was made according to the Bethesda system 2014. Colposcopic evaluation included: Direct examination of cervix with green filter and saline application, examination of the cervix after application of 3% acetic acid, seeing the junction of squamous cell, erosion, papillary lesions, aceto-white areas and vascular design, examination of the cervix after Lugol test in which normal squamous epithelium, which contains glycogen, it turns brown. The colposcopic findings were classified according to Modified Reid's Colposcopic Index. Cervical biopsy was taken from the most suspicious area detected by acetowhite staining and lugol's iodine by punch biopsy forceps. Colposcopy directed biopsies were processed. Biopsy specimens were received in 10% formalin fixative. Histopathological slides prepared and stained with hematoxylin and eosin and examined under a light microscope.

Data analysis:

All data was collected on predesigned Proforma & entered in master chart.

Appropriate statistical formulas were applied.

Results:

Table 1: Distribution of cases based on symptoms:

SYMPTOMS	(No.)	PERCENTAGE %
Persistent vaginal discharge	79	79%
Postcoital Bleeding	14	14%
Intermenstrual Bleeding	12	12%
Low Backache	50	50%
Postmenopausal Bleeding	05	05%

The commonest presenting symptom was vaginal discharge (79% of the patients). Other presenting symptoms were low backache (50%), postcoital bleeding (14%), intermenstrual bleeding (12%) and postmenopausal bleeding (05%)

Table 2: Distribution of cases based on Pap smear findings

PAP SMEAR	NO. OF WOMEN (N=100)	PERCENTAGE
Normal	-	-
Inflammatory	82	82%
ASCUS	07	07%
LSIL	09	09%
HSIL	01	01%
MALIGNANT CELLS	01	01%

Pap smear revealed that 82% of the studied population had inflammatory smear & 18% had a positive Pap smear. The result of Pap smear was considered positive if it revealed ASCUS, LSIL, HSIL & MALIGNANT CELLS. Among 10% positive cases, there were 3% ASCUS, 5% LSIL, 1% HSIL & 1% showed Malignant cells.

Table3: Distribution of cases based on Colposcopy findings:

Findings	NUMBER OF CASES	PERCENTAGE %
Normal	-	-
Inflammatory	62	62%
CIN 1	25	25%
CIN 2	11	11%
CIN 3	02	02%

On Colposcopy, 62 patients were found to have findings consistent with inflammation. Colposcopy findings suggestive of CIN-1 CIN-2 were observed in 25% and 11% patients respectively. Two patients showed colposcopic findings of CIN-3. Colposcopic results were taken positive from CIN-1 onwards.

Table 4: Distribution of cases based on Cervical Biopsy findings:

BIOPSY	FREQUENCY	PERCENTAGE
CERVICITIS	71	71%
CIN-1	22	22%
CIN-2	05	5%
CIN-3	01	1%

Squamous cell carcinoma	01	1%
Total	100	100

All of the 100 cases underwent colposcopic directed biopsy. Biopsy was taken from the most abnormal areas. 71% of the patients showed features of cervicitis. 22% and 5% of the patients showed findings of CIN-1 and CIN-2 respectively. One patient had features of CIN-3 and 1 case had findings of Squamous cell carcinoma.

Table 5: Correlation between PAP Smear and Cervical Biopsy (n=100)

PAP SMEAR		CERVICAL BIOPSY FINDINGS				
FINDINGS	NUMBER	CERVICITIS	CIN 1	CIN 2	CIN 3	SCC
NORMAL	-	-	-	-	-	-
INFLAMMATORY	82	66	14	02	-	-
ASCUS	07	05	02	-	-	-
LSIL	09	-	06	03	-	-
HSIL	01	-	-	-	01	00
MALIGNANT CELLS	01	-	-	-	-	01
TOTAL	100	71	22	05	01	01

In the population studied, 13 Patients out of 100 were positive on Pap smear. Positive PAP smears were taken from ASCUS onwards.

29 Patients out of 100 were positive on Cervical Biopsy. The positive result for cervical biopsy was taken from CIN-1 onwards. Pap smear was positive in 13% cases out of Biopsy proven 29% cases.

Table 6: Comparison of PAP Smear with Cervical Biopsy:

PAP SMEAR	BIOPSY		
	POSITIVE	NEGATIVE	TOTAL
POSITIVE	TP 13	FP 05	18
NEGATIVE	FN 16	TN 66	82
			100

Out of 18 patients that were positive for PAP Smear, 13 were identified as True Positives and remaining 5 were False Positives whereas out of 82 Negatives, 16 patients were false negatives & 66 patients were true negatives.

The sensitivity of PAP smear is 44.8% and the specificity is 92.9%. The Positive Predictive Value of PAP Smear is 72.2% and the Negative Predictive Value is 80.4%. The Accuracy of PAP Smear is 79%.

Table 7: Correlation between Colposcopy and Cervical Biopsy:

COLPOSCOPY		CERVICAL BIOPSY				
FINDINGS	NUMBER	CERVICITIS	CIN 1	CIN 2	CIN 3	SCC
Normal	-	-	-	-	-	-
Cervicitis	62	58	04	00	00	00
CIN 1	25	13	12	00	00	00
CIN 2	11	00	06	05	00	00
CIN 3	02	00	00	00	01	01
TOTAL	100					

On Colposcopy out of 100 patients, 62% showed features of cervicitis while on cervical biopsy only 58% were proved to be cervicitis and the remaining 4% cases showed CIN-1.

Colposcopy and Cervical Biopsy results were taken positive from CIN-1 onwards. Negative results involved Normal findings and findings suggestive of Cervicitis.

Table 8: Comparison of Colposcopy with Cervical Biopsy

COLPOSCOPY	CERVICAL BIOPSY		TOTAL
	Positive	Negative	
Positive	TP – 25	FP – 13	38
Negative	FN – 04	TN – 58	62
			100

Out of the studied population colposcopy showed 38% were positives out of which 25% were true positives and 13% were false positives. A total of 62% were negatives, 04% being false negatives and 58% were true negatives. The Sensitivity of Colposcopy is 86.2% and the Specificity was 81.6%. The positive predictive value is 65.7% and the negative predictive value is 93.5%. The Accuracy of Colposcopy is 83%.

Of the remaining 38 patients 25 patients showed CIN-1 changes on colposcopy, 13 patients were confirmed to have cervicitis on biopsy and the rest that it 12 confirmed CIN-1 on cervical biopsy.

A total of 11 Patients were positive for CIN-2 on Colposcopy however only 5% were positive for CIN-2 on Cervical Biopsy and the rest 6 patients had features of CIN-1 on Biopsy.

2 patients out of the studied population showed features of CIN-3 on Colposcopy, out of which one was CIN-3 and the other one proved as Squamous cell carcinoma on Cervical Biopsy.

Out of the studied population colposcopy showed 38% were positives out of which 25% were true positives and 13% were false positives.

Discussion:

The commonest presenting symptom was **Persistent vaginal discharge** (79% of the patients). Other presenting symptoms were low backache associated with white discharge (50% of the patients), postcoital bleeding (14%), intermenstrual (12%) and postmenopausal bleeding (5%). The results of our symptoms were similar to **Deshpande Sonali et al.**⁽⁸⁾

In our study PAP smear was taken for all patients, 82% showed inflammatory atypia, 7% showed ASCUS, 9% showed LSIL, 1% showed HSIL & 1% showed Malignant cells. Out of 18 patients that were positive for PAP Smear, 13 were identified as True Positives as they were positive on biopsy also and remaining 5 were False Positives whereas out of 82 Negatives, 16 patients were false negatives & 66 patients were true negatives.

In mild dysplasia, the correlation was poor between Cyto&Histo-pathology, whereas it was good for moderate to severe dysplasia.

In the current, the PPV was 40%, NPV was 93 % and accuracy was 88%.

Vidya Rani SM et al in 2017 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.⁽⁹⁾

Goel A et al performed “a study which showed the sensitivity of Pap smear was 50% and specificity was 92.4%⁽¹⁰⁾. The positive predictive value was found to be 84.2%, negative predictive value 74.07% and accuracy 76%”. This shows that Pap smear is less sensitive as a screening method. In cases of clinically unhealthy cervix even with normal cytology colposcopy has to be used for confirmation. Out of the studied population colposcopy showed 38% were positives out of which 25% were true positives and 13% were false positives.

A total of 62% were negatives, 04% being false negatives and 58% were true negatives. The Sensitivity of Colposcopy is 86.2% and the Specificity was 81.6%. The positive predictive value is 65.7% and the negative predictive value is 93.5%. The Accuracy of Colposcopy is 83%.

Vidya Rani SM et al in 2017 conducted a study which showed 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%. **Massad et al**⁽¹¹⁾ reported sensitivity of 89%. “Specificity reported in various studies differed widely from 15% to 87% which may be explained by difference in the inclusion criteria adopted in various studies. Studies with similar inclusion criteria have reported comparable sensitivity values. Low specificity of Colposcopy can be explained when compared to Pap smear due to the high incidence of unsuspected Aceto-White epithelium which might be due to inflammation, immature metaplasia, and latent HPV infections”⁽¹¹⁾.

Conclusion: The commonest presenting complaint was Persistent vaginal discharge (69% of the patients). Among the 100 PAP smear were taken 82% showed inflammatory atypia, 7% showed ASCUS, 9% showed LSIL, 1% showed HSIL and 1% showed Malignant cells. Among the 100

cases studied for Colposcopy & interpreted on the basis of Reid's Colposcopic Index, 62 patients were scored as Inflammatory while 25 patients depicted the features of CIN-1, 11 had features of CIN-2 and 2 patients were CIN-3. On Cervical Biopsy 71% proved to be cervicitis, 22% as CIN-1, 5% as CIN-2, 1% showed CIN-3 and 1% was Squamous cell carcinoma. The sensitivity and specificity of Pap smear and Colposcopy is 45% and 93.3%, and 88.23% and 86.3%, respectively.

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