

# ROLE OF CYTOLOGY AND COLPOSCOPY DIRECTED BIOPSY IN EVALUATION OF CLINICALLY SUSPICIOUS CERVIX

By

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## ABSTRACT

**Background:** Cervical cancer is the second most common cancer among women in developing countries. Cervical cancer is a deadly disease once it reaches the invasive stages but out of all the female genital tract cancers, it is the only preventable cancer if detected in its early stages and the disease is almost 100% curable with accurate screening and early detection. Traditional screening for cervical cancer is done with papanicolaou smear test, colposcopic examination and colposcopic directed biopsy for histopathology.

**Objective:** To evaluate efficacy of both cytology and colposcopy directed biopsy in evaluation of clinically suspicious cervix.

**Patients and Methods:** Cross sectional study on 300 patients with clinically suspicious cervix attending the outpatient Department of Obstetrics and Gynecology, at the Hospital of Al-Azher Assiut University.

**Results:** Pap smear had a sensitivity of 25.5% and a specificity of 87% which was attributed to the high number of false negative smears. Accuracy of pap smear was 76.7%.

Colposcopy showed a sensitivity of 82% and a specificity of 81%. Sensitivity was more than pap smear but specificity was less than pap smear. \* Accuracy of colposcopy was found to be 81% which was comparatively more than that of pap smear (77%).

**Conclusion:** It is evident that 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. Both the result of cytology and colposcopy should be compared to those of histopathology, that histopathology remain the main method of diagnosing the precursors of neoplastic cervical lesion.

**Key word:** Pap smear, Colposcopy, Histopathology, Suspicious cervix.

## INTRODUCTION

Globally, cervical cancer comprises 12% of all cancer in women .Cervical cancer is the second most common cancer among women in developing countries (Ferlay *et al.*, 2013).

Cervical Inter Epithelial Neoplasia (CIN) is not cancer and is usually curable if detected in its early stages with accurate

screening and early detection. Most cases of CIN either remain stable or are eliminated by the person's immune system without need for intervention. However, a small percentage of cases progress to cervical cancer, typically cervical squamous cell carcinoma (SCC), if left untreated (Tainio *et al.*, 2018).

Traditional screening for cervical cancer is done with papanicolaou smear test, colposcopic examination and colposcopic directed biopsy for histopathology, Pap smears have formed the basis of cervical cancer screening and detection programs for many years. National cytology-based screening programs have contributed substantially to the marked decline in deaths from cervical cancer in these countries (ACOG, 2016).

Colposcopy practice includes the complete colposcopy visit from visual assessment of the cervix to biopsy sampling if indicated. Colposcopy should be viewed as a risk assessment tool that directs subsequent management with biopsies, treatment, or observation. When a lesion(s) is/are present, colposcopy-directed biopsies of 2 to 4 sites are taken to establish a histopathologic diagnosis of the most severe disease present, confirm a lack of CIN/SIL/cancer, or assess for possible therapy. For low-risk women with a normal colposcopic impression, deferring biopsies may be acceptable (Wentzensen *et al.*, 2017).

## PATIENTS AND METHODS

The present cross sectional study was carried out on 300 patients, attending the outpatient Department of Obstetrics and Gynecology, at the Hospital of Al-Azhar (Assiut) University

The patients were selected by selective screening presence of either one or more of the following Criteria of clinically suspicious cervix:

- White or red patches.
- Polyp.
- hypertrophied cervix.

- Ulcers.
- Endocervical purulent discharge.
- Nodular cervix with retention cyst.

### Inclusion criteria:

Women in age group of 20-60 years associated with:

1. Persistent vaginal discharge
2. Post coital bleeding
3. Cervical hypertrophy
4. Cervical erosion/ ulceration/ growth/ oozing surface
5. Contact bleeding
6. Cervix flushed with petechial spot
7. Unexplained occasional foul smelling discharge per vagina.

### Exclusion criteria:

1. Pregnant or postpartum or post abortive patients.
2. Patient having any history of treatment for either cervical dysplasia or vulval warts.
3. Patient who had underwent to recent endometrial curettage, hysterosalpingography, cervical biopsy or hysterectomy.
4. Immunocompromised patients (HIV patient on corticosteroids).

### All patients were submitted to:

1. Written informed consent and counseling.
2. History.
3. Physical examination.
4. Local examination of vulva.

5. Speculum examination of cervix and vagina.
6. Cytological methods by Cervical cytology:

This is the most efficient single method of detecting premalignant and clinically unsuspected invasive cancers of the cervix. The cervical scrape was obtained under direct vision with the vaginal speculum in position (The Ayre's spatula was inserted into the os and the spatula gently bit firmly rotated through 360 degree). We used the other side of spatula to obtain the exfoliated cells from the posterior fornix. We used the cytobrush to obtain the exfoliated cells from endocervix.

The cervical mucus and cellular material on the spatula was spread evenly across a glass slide, the frosted end of which has been previously labeled in pencil with the patient's name. The slide was fixed immediately by immersing it in a solution of 95% ethanol. It was left in the fixative for 30 minutes, following which it was safely stored by dry at room temperature. Cervical smears was received in the laboratory ready-fixed and stored at room temperature. By convention a modified Papanicolaou stain was used to the slide.

#### **Colposcopic technique:**

Cervix was examined under illumination after cleaning the vagina and cervix with cotton swabs dipped in Normal Saline in order to remove the discharge.

**Colposcopy directed biopsy:** was taken from the abnormal site. When the acetowhite (AW) lesion was homogenous, a site near the new squamo-columnar junction (SCJ) was selected as it was more likely to harbor the worst abnormality. In heterogeneous (AW) lesion, the most suspicious area was biopsied. In cases where the new SCJ was not visualized fully as in postmenopausal women, endocervical curettage was done. The specimen was preserved in 10% formalin, labeled and sent for HPE examination.

All 300 patients underwent pap smear; colposcopic examination and colposcopy directed biopsy.

#### **Statistical analysis:**

Statistical analysis was performed using Statistical package for social science (SPSS) version 25.

**The following tests were used:** Descriptive analysis of the results in the form of percentage distribution for qualitative data (minimum, maximum, mean and standard deviation) calculation for quantitative data.

- P value was considered significant when  $P \leq 0.05$ .

## RESULTS

As age increased, prevalence of CIN also increased. Prevalence of CIN was found to be high among the age group 30-49 years. 2% of women had contact with more than one partner, out of them 3.9% had CIN. 3% of husbands of women in the study group had history of promiscuity. Out of them, no women had CIN. There was high prevalence of CIN, when the

duration of marriage increased and hence the duration of exposure to sexual intercourse. Among the study group, 8% were para 1, among them 5.9 had CIN. 34% were para 2 and out of them 37.3% had CIN. 38% were para 3, among them 39.2% had CIN. 20% were para 4 or more, among them 17.6% had CIN (**Table 1**).

**Table (1): Result of age , sex , duration of marriage and parity**

Parameters		Total cases (n=300)		CIN cases (n=51)	
		No.	%	No	%
Age	20-29	39	13	1	2
	30-39	114	38	20	39.2
	40-49	93	31	18	35.3
	50-60	54	18	12	23.5
Sex	Wife	6	2	2	3.9
	Husband	9	3	0	0
Duration of marriage	< 5 yrs	39	13	1	2
	5-10 yrs	105	35	7	13.7
	11-20 yrs	96	32	23	45.1
	> 20 yrs	60	20	20	39.2
Parity	1	24	8	3	5.9
	2	102	34	19	37.3
	3	114	38	20	39.2
	>4	60	20	9	17.6

The common complaints were; white discharge and bleeding PV, which was either post coital, intermenstrual or of post-menopausal type. Out of the 56% of patients who complained of white discharge 70.6% had CIN. Of the 7% who complained of post coital bleeding 11.8% had CIN. 11% (had intermenstrual bleeding, among them 7.8% had CIN. 5% had post-menopausal bleeding, out of them 9.8% were diagnosed to have CIN.

Other complaints included loss of weight, loss of appetite, UTI, lower abdominal pain. Among them, none had CIN. Among women with ectopy cervix, 58.8% had CIN, among those with congestion alone 11.8% had CIN, among those with hypertrophy and congestion 11.8% were found to have CIN, and in those who had hypertrophy with ectopy 17.6% were CIN positive. All polyps were benign (**Table 2**).

**Table (2): Result of Complaints and Clinical appearance of cervix**

Parameters		Cases	Total Cases		CIN Cases	
			No.300	%	No.51	%
Complaints	White discharge	168	56	36	70.6	
	Post coital bleeding	21	7	6	11.8	
	Intermenstrual bleeding	33	11	4	7.8	
	Post menopausal bleeding	15	5	5	9.8	
	Loss of weight/appetite	15	5	0	0	
	Others	48	16	0	0	
	Total	300	100	51	100	
Clinical appearance of cervix	Atrophy	7	2.5	0	0	
	Congestion	47	15.5	6	11.8	
	Ectopy cervix	176	58.6	30	58.8	
	Hypertrophy + congestion	19	6.3	6	11.8	
	Hypertrophy + ectopy	36	12	9	17.6	
	Polyps	15	5	0	0	
	Total	300	100	51	100	

Pap smear was done at 300 patients. 5% of smears were found to be normal, 80% showed inflammatory atypia, 10.7%

showed mild dysplasia, 4.3% showed moderate dysplasia (Table 3).

**Table (3): Result of Pap Smear Findings**

Findings	No. of cases 300	%
Normal	15	5
Inflammatory atypia	240	80
Mild dysplasia	32	10.7
Moderate dysplasia	13	4.3
Severe dysplasia	0	0
Invasive cancer	0	0

Among the 300 cases studied, 29.3% (89/300) were diagnosed as colposcopically abnormal. Among the abnormal cases, AW areas were diagnosed in 17.7%. Punctate pattern of vessels was

seen in 8% of cases and mosaic pattern of vessels was diagnosed in 4% of women. And they all underwent colposcopic guided biopsy for histopathology (Table 4).

**Table (4): Result of Colposcopic appearance of cervix**

Appearance	No. of cases	%
Normal	7	2.3
Ectopy cervix	93	31
Inflammatory changes	48	16
Polyps	15	5
Leucoplakia	6	2
Aceto White (AW) areas	53	17.7
Punctate pattern	24	8
Mosaic pattern	12	4
Atypical vessels	0	0
Unsatisfactory	42	14
Total	300	100

Results of 300 cases were subjected to colposcopically directed biopsy. Majority of cases, 46.1% had chronic cervicitis, 27% had chronic cervicitis with ectopy,

2.3% had ectopy cervix, 2.3% had epithelial hyperplasia, 5.4% had benign polyp, 10% had mild dysplasia, 7% had moderate dysplasia (**Table 5**).

**Table (5): Result of histopathological findings(HPE)**

HPE	No. of cases	300	%
Chronic cervicitis	138		46.1
Chronic cervicitis + ectopy	81		27
ectopy cervix	7		2.3
Epithelial hyperplasia	7		2.3
Polyp (Benign)	16		5.4
Mild dysplasia	30		10
Moderate dysplasia	21		7
Severe dysplasia	0		0

Comparison between Pap smear and colposcopic appearance with histopathological findings were presented:

**Table (6) & (7)**. Also, comparison between efficacy of Pap smear and colposcopy was presented: **Table (8)**.

**Table (6): Comparison of Pap smear with Histopathological findings results**

Pap smears	No.	Histopathological findings									
		Normal		CIN I		CIN II		CIN III		Total	
		No.	%	No.	%	No.	%	No.	%	No.	%
Normal/ inflam. Atypia	255	217	85.1	25	9.8	13	5.1	0	0	38	14.9
Mild Dysplasia	32	27	84.3	5	15.7	0	0	0	0	5	15.7
Moderate Dysplasia	13	5	38.5	0	0	8	61.5	0	0	8	61.5
Severe Dysplasia	0	0	0	0	0	0	0	0	0	0	0
Total dysplastic Smears	45	32	71.1	5	11.1	8	17.8	0	0	13	28.9

**Table (7): Comparison of Colposcopic appearance with Histopathological Findings results**

Colposcopic findings		No	Histopathological findings				
			Normal	CIN I	CIN II	CIN III	Inv. CA
Normal / unsatisfactory		211	202	6	3	0	0
Abnormal	AW	53	38	10	5	0	0
	Punctate	24	8	8	8	0	0
	Mosaic	12	1	6	5	0	0
	Atypical vessels	0	0	0	0	0	0
Total		300	249	30	21	0	0

**Table (8): Efficacy of Pap smear and colposcopy**

Test	True positive	False positive	True negative	False negative	Sensitivity	Specificity	PPV	NPV	Accuracy
Pap smear	13	32	217	38	25.5	87	29	85	76.7%
Colposcopy	42	47	202	9	82	81	47	96	81%

### DISCUSSION

Cervical cancer was the second most frequent cancer worldwide, However, invasive cancer of the cervix was considered to be a preventable condition as it was associated with a long pre invasive stage (CIN) making it amenable to screening and treatment.

In the present study screening was done in 300 women with unhealthy cervix, and women with dysplastic smears, with colposcopy and its results were correlated with pap smear and biopsy to determine the sensitivity and specificity of these methods in detecting CIN.

Regarding age distribution, high prevalence of CIN was found among the age group of 30-49 years with mean age of 41 years which was seen in 37% of cases. *Vaidya (2012)* showed in his study that CIN was more prevalent in the age group of >35 years.

Increasing number of sexual partners had the effect on increasing the risk of developing CIN and invasive disease. In our study, only 2% of women revealed the history of multiple sexual partners, out of which 3.9% had CIN. In our study, though 3% of males had multiple sexual partners, none of their wives developed CIN.

Sex with high risk males was also another risk factor for the development of CIN (*Becker et al., 2013*).

Duration of marriage and duration of exposure to sexual intercourse had a distinct role in genesis of cervical dysplasia. In our study, the prevalence of CIN was .45.1 % in women who were married for 11-20 years, and 39.2% among women who were married for >20years. *Vaidya (2012)* 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.

Regarding parity, our study showed increased prevalence of CIN among multiparous women. 37.3 % were para 2, 39.2 % were para 3 and 17.6% were para 4 or more. *Vaidya (2012)* showed more positive cases of CIN were found with parity more than 4. This might be attributed to hormonal and nutritional changes that occur in pregnancy, Immuno suppression during pregnancy, and cervical trauma during vaginal delivery.

Among the complaints, majority of women (56%) complained of excessive white discharge per vagina. Among them CIN was found in 70.6% .Excessive vaginal discharge playing a role in contributing to the development of CIN was also proved to be a risk factor in the study conducted by *Vaidya (2012)*. In their study, 24% had vaginal discharge.

Regarding the clinical appearance of cervix, the most common finding was ectopy cervix where the squamous

epithelium of ectocervix was replaced by the columnar epithelium of endocervix. Ectopy was seen in 58.6%, rest of patients showed congestion in 15.5%, Hypertrophy with congestion seen in 6.3%, Hypertrophy with ectopy was seen in 12% and polyp was found in 5% of cases.

CIN was found in 11.8% in women who showed congestion, 58.8% in women who showed ectopy and 11.8 % in women with hypertrophy + Congestion and 17.6% in women with hypertrophy + ectopy.

Pap smear was taken for 300 cases. It showed mild dysplasia in 10, 7%, moderate dysplasia in 4.3%. Sensitivity of pap smear was found to be very low – 25.5% compared to its specificity which was 87%. This was attributed to the high number of false negative smears.

This data suggested that with colposcopy as a screening tool, the rate of false negative cytology could be significantly reduced. Colposcopy enhanced cervical screening particularly in women with otherwise negative smears. colposcopy Sensitivity was found to be 82% and specificity was 81%. This showed a high sensitivity and a low specificity when compared to Pap smear. That was due to the high incidence of unsuspected Aceto White (AW) epithelium which might be due to inflammation, immature metaplasia, erosion and latent HPV infections. Out of 53 cases which showed AW areas without any vascular pattern only 18 were confirmed by biopsy.

Colposcopy and biopsy were positive in 82.4% of cases while pap smear and biopsy were positive in only 25.4% of cases. This indicated the usefulness of

colposcopy in diagnosing lesions missed by pap smear

## **CONCLUSION**

Earlier diagnosis of CIN in adult women is a desirable goal. Invasive cancer of cervix is considered to be preventable since it is associated with a long pre – invasive stage (CIN) making it amenable to screening and treatment.

Papanicolaou (pap) smear is still primary method of screening for cervical cancer in our locality .This is due to the fact that it can detect early dysplastic cell changes and women with such abnormalities can be subjected to further diagnostic testing and treatment.

Colposcopy in general has a role in the evaluation of women with abnormal pap smears, unhealthy cervix, and seems to be more accurate in detecting CIN. Hence, primary colposcopy may be incorporated into genito urinary tract screening at first visit.

From the results of this study, it is evident that 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.

## **RECOMMENDATIONS**

The current study recommends that cervicovaginal smears should be taken for all cases of clinically suspicious cervix, and those having abnormal Pap smear should be referred to colposcopic examination. Both the result of cytology and colposcopy should be compared to those of histopathology, that histopathology remain the main method of



diagnosing the precursors of neoplastic cervical lesion.

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## دور الفحص الخلوي وفحص منظار عنق الرحم الموجه بسحب عينة لتقييم عنق الرحم المشكوك فيه في الفحص السريري

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**خلفية البحث:** يعد سرطان عنق الرحم ثاني أكثر أنواع السرطان شيوعاً بين النساء في الدول النامية، فسرطان عنق الرحم هو مرض مميت بمجرد أن يصل إلى المراحل المتقدمة؛ ولكن من جميع السرطانات التناسلية الأنثوية، هو السرطان الوحيد الذي يمكن الوقاية منه إذا تم اكتشافه في مراحله المبكرة. و من الممكن منع الوفيات الناجمة عن سرطان عنق الرحم من خلال برامج للفحص والاستكشاف المبكر والعلاج الذي يتضمن إجراء الفحص الخلوي باستخدام اختبار مسحة عنق الرحم ومنظار عنق الرحم وعينة موجه بمنظار عنق الرحم وتحليلها باثولوجيا.

**الهدف من البحث:** تقييم فاعلية كلا من الفحص الخلوي ومنظار عنق الرحم الموجه بعينة للفحص الباثولوجيا كطرق تحرى لتقييم عنق الرحم المشكوك فيه في الفحص السريري.

**المريضات وطرق البحث:** تمت هذه الدراسة على 300 حالة من السيدات اللواتي تم تقييمهن بفحص عنق الرحم المشكوك فيه اثناء الفحص السريري اللواتي حضرن بالعيادة الخارجية لقسم النساء والتوليد بمستشفى الأزهر الجامعي فرع اسيوط.

**نتائج البحث:** ابلغت نتيجة مسحة عنق الرحم عن حساسية تتراوح 25.5% ولكن تحديدها 78%، ودقة 76.7%.

أبلغ منظار عنق الرحم عن حساسية تتراوح ب 82 %، ولكن تحديدها 81 %، ودقة تصل الى 81%.

**الاستنتاج:** منظار عنق الرحم أكثر حساسية دقة وسرعة في تشخيص المرض واكثر فعالية في تحديد بداية الاورام عن اختبار مسحة عنق الرحم وبناء عليه فان ازدواج الطريقتين ومنظار عنق الرحم والفحص الخلوي يضاعف من دقة النتائج وحساسية تحديد المرض في برامج مسح عنق الرحم ومقارنة نتيجتهما بنتيجة تحليل عينة الباثولوجيا التي تثبت انها الوسيلة الاساسية لتشخيص امراض عنق الرحم.