

# A Comparative Study between Colposcopy versus Histo and Cytopathology as Diagnostic Tools for Detection of the Causes of Post Contact Bleeding

Mai Ahmed Gobran\*, Safaa AbdelSalam Ibrahim, Sabah Mohamed Hanafy

Department of Pathology, Zagazig University, Egypt

## Abstract

Postcontact Bleeding (PCB) is defined as bleeding occurring during or immediately after cervical contact as sexual intercourse, vaginal examination and vaginal douches at a time separate from menstruation. It is a common, multifactorial, gynecological symptom. In a review of PCB, the point prevalence of PCB among women in the community ranged from 0.7% to 9%. Occasionally, it is the first presentation of precancerous cervical lesions, and the prevalence of PCB in women with cervical cancer has been reported to vary between 0.7% and 39%. Cervical cytology is used to evaluate women with PCB, and colposcopy is usually performed when there is abnormal cytology. The current management of PCB is not constant. Colposcopy is an important component of the cervical screening program, but there are several disadvantages for patients with PCB undergoing colposcopy screening; for example, patient anxiety and undue distress, use of valuable colposcopy time, and the progression to unnecessary interventions.

The aim of this study was to evaluate women with PCB using clinical examination, cytology, colposcopy, and pathology in order to know the accuracy of each and all in determining the causes of bleeding.

This study included fifty women with Post-Contact Bleeding (PCB).

Each woman was asked about the following full history taken: complete history taking, clinical examination, cytological examination, colposcopic examination and colposcopically-guided punch biopsy.

Our results showed that:

Forty patients (80%) belonged to the sexually active reproductive age group, only 2 patients (4%) were below 20 years and 3 patients (6%) were postmenopausal. Postcontact bleeding was infrequently seen in nulliparas i.e. 2 patients (4%), primiparous in 4 patients (8%) and 44 patients (88%) were multiparas. All patients were non-smoker and non-alcoholic. None of the 50 patients was pregnant and all patients belonged to low socioeconomic status. All women had undergone cytological examination. Cytology identified 6 patients (12%) only with LGSIL and 3 patients (6%) with HGSIL.

Colposcopy revealed atypical transformation zone in 15 patients (30%). Majority of patients i.e. 34 patients (68%) had typical transformation zone and only one patient (2%) had unsatisfactory colposcopic findings. Vascular ectopy was detected in 15 patients (30%). Colposcopically directed biopsies were obtained in total of 16 patients (32%) of all patients who had an atypical transformation zone in 15 patients (30%) and unsatisfactory colposcopy in one patient (2%). Histological examination of obtained biopsies revealed that: Five patients (10%) had viral changes with CIN I, two patients (4%) had CIN II, one patient (2%) had CIN III and eight patients (16%) had chronic cervicitis. Colposcopy had a positive predictive value of 50% i.e. 8 of 16 patients had a positive histopathology. Sensitivity of colposcopy was 88% and specificity was 79%. Cytology had a positive predictive value of 53% i.e. 8 of 15 patients had a positive histopathology. Sensitivity of cytology was 57% and its specificity was 84%. On comparison between colposcopy and cytology: Colposcopy (88%) was more sensitive than cytology (57%). Cytology (81%) was more specific than colposcopy (79%). Predictive values of positive results were comparable i.e. colposcopy was 50% and cytology was 53%.

## Keywords

CIN • LGSIL • HGSIL • Papanicolaou smear

## Abbreviations

PCB: Post Contact Bleeding; CIN I: Cervical Intraepithelial Neoplasia grade 1; CIN II: Cervical Intraepithelial Neoplasia grade 2; CIN III: Cervical Intraepithelial Neoplasia grade 3; Pap smear: Papanicolaou smear; LGSIL: Low Grade Squamous Intra-Lesion; HGSIL: High Grade Squamous Intra-Lesion

\*Address for Correspondence: Mai Ahmed Gobran, Department of Pathology, Zagazig University, Egypt; Tel: +201063477990; E-mail: magibran@medicine.zu.edu.eg

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## Introduction

Post Contact Bleeding (PCB) is defined as non-menstrual bleeding that occurs following intercourse, vaginal examination and vaginal douches. PCB has many causes, the most serious being precancerous cervical lesions. Colposcopy referral for every case of PCB is important. The main aim of investigating PCB is to exclude precancerous cervical lesions [1].

Post Contact Bleeding (PCB) has an annual cumulative incidence of 17% and 6% respectively in menstruating women from a questionnaire study based on subjects within urban English, general practice setting. PCB occurs in 0.7-39% of women with cervical cancer. The risk of a woman seen in the community with PCB having cervical cancer is approximately 1 in 44,000 in 20-24 year olds and one in 2,400 in 45-54 year olds [2].

Cytology evaluates the morphological changes in the exfoliated cells while colposcopy evaluates mainly the changes in the terminal vascular network of the cervix which reflect the biochemical and metabolic changes in the tissues. Colposcopy is very accurate in differentiating between invasive and non invasive lesion and in differential diagnosis between inflammatory atypia and neoplasia. When colposcopy and cytology are combined the diagnostic accuracy is near 100%. So the better results are got by combination of both methods. Cervical cytology and colposcopy are

used to evaluate women with PCB, and histopathological examination is the final route of diagnosis of precancerous cervical lesions [3].

### Aim of the work

The aim of this study is to evaluate women with postcontact bleeding using clinical examination, cytology, colposcopy, and pathology in order to know the accuracy of each and all in determining the causes of bleeding.

## Patients and Methods

This study was carried in Outpatient Obstetric and Gynecologic Clinic, Zigzag university hospitals during the period from 2018 to 2020. The research team was made up of gynecologists and pathologists. The study included fifty women with Post-Contact Bleeding (PCB) who met all the inclusion criteria, recruiting with their age or parity limit.

### Inclusion criteria

- All women presented at Gynecology Outpatient Clinic with post contact bleeding.
- Aged 20-65 years.
- Any parity.
- Sexually active women.

### Exclusion criteria

- Pregnant women.
- Women with bleeding due to vulvovaginitis, acute cervicitis or polyps.
- Women unwilling to cooperate in the study.
- Women with frank evidence of invasive cervical carcinoma.
- Women with prior total hysterectomy.

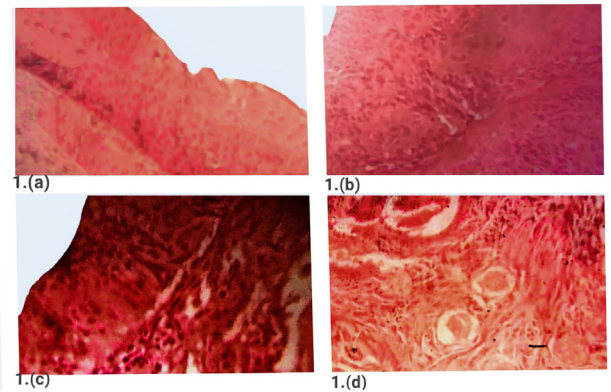
### Methods

Each woman was asked about the following full history taken:

1. Personal history, including: age of the patient, age of marriage and its duration.
2. Main complaint which is post contact bleeding and its duration.
3. Menstrual history.
4. Obstetric history.
5. Contraceptive history including the type and duration of use.
6. Past history of medical problems and surgical procedures she had, especially cervical surgery as previous cauterization.
7. Family history of similar condition or cancer cervix.
8. Husband history for smoking and venereal diseases.
9. History of sexually transmitted diseases

### Methodology

I- Clinical examination: After obtaining a history, the participant moved to the examination table to be examined by the researcher, a bivalve disposable speculum was inserted into the vagina, and the vulva, vaginal walls and the cervix were inspected with comment on the morphology and any apparent lesion seen Figures 1a-1d.



**Figure 1.** (a): histopathology picture of normal cervical epithelium ( $\times 100$ ,H&E);1. (b): histopathological image of CIN Low grade;with atypical changes with nuclear pleomorphism and hyperchromatism affecting lower one third of cervical epithelium( $\times 100$ ,H&E);1(c):histopathological image of CIN High grade;with marked atypical changes with nuclear pleomorphism and hyperchromatism affecting more than two third of cervical epithelium( $\times 100$ ,H&E);1. (d):histopathological image of well differentiated squamous cell carcinoma with formation of cell nests of malignant squamous epithelial cells showing extensive nuclear pleomorphism and hyperchromatism & central keratin whorls invading basement membrane of epithelium & infiltrating the cervical submucosa( $\times 100$ ,H&E);

II- Cytological examination: The smears were taken by cervical scraping using Ayres spatula in the majority of participant, while cytobrushes were reserved for use in women with nulliparous os. The specimen was applied on the slide and immersed immediately in 95% ethyl alcohol for at least 30 minutes. Thereafter, the slide was sent to the pathologist for staining and examination.

Papanicolaou smears showing atypia with viral changes, mild, moderate or severe dyskaryosis and carcinoma in situ were considered positive cytology. Metaplastic changes, inflammatory smears and inflammatory atypia without viral changes were considered negative cytology.

Using the Bethesda system, patients with viral changes and mild dyskaryosis were be graded as Low-Grade Squamous Intraepithelial Lesion (LG-SIL) and those with moderate to severe dyskaryosis and carcinoma in situ were graded as High-Grade Squamous Intraepithelial Lesion (HG-SIL).

III- Colposcopic examination: Patients were evaluated colposcopically. The abnormal colposcopic evidence of lesions is acetowhite areas, abnormal angioarchitecture, punctuations, mosaic pattern and gland openings.

Colposcopy is indicated in all cases with postcontact bleeding and positive papsmear as:

- Atypical Squamous Cells of Undetermined Significance (ASCUS).
- Human Papilloma Virus (HPV).
- Low-Grade Squamous Intraepithelial Lesion (LGSIL).
- High-Grade Squamous Intraepithelial Lesion (HGSIL).
- Malignant cells.

According to colposcopic examination, the patients were classified into two groups:

- 1) Normal colposcopic findings.
- 2) Abnormal colposcopic findings:
  - a. Significant colposcopy, which showed different colposcopic lesions,

vascular changes and gave us the possibility that CIN lesions I, II and III were found in biopsies.

b. Highly significant colposcopy, which showed suspicious colposcopic lesion usually with vascular changes and gave us the possibility that an early precancerous cervical lesion was found in biopsies.

c. Unsatisfactory colposcopy, which showed colposcopic changes showing an atypical transformation zone grades 1-3 (according to grade of clarity of demarcation), and suspect invasive cancer was considered positive colposcopy.

In cases of unsatisfactory colposcopy, two tablets of 200 µg misoprostol (400 µg Cytotec) were inserted into the posterior vaginal fornix and the patients were observed in the hospital for 6 hours and the side effects of the drug were noted such as abdominal pain, perception of increase in body temperature, vaginal bleeding, headache or vomiting before a colposcopic re-examination .

I- Colposcopically-guided punch biopsy: It was obtained by punch biopsy forceps from suspicious areas wherever these were located. One or more biopsies were obtained from each patient. Specimens were preserved with 10% formalin solution and were sent for examination by pathologist.

The results were obtained, tabulated and statistically analyzed. In the aim of evaluating and comparing the accuracy of cytology and colposcopy, the sensitivity and specificity, the predictive value for positive test results and for negative test results, and the percentages of false-positive results and false-negative results were calculated for Pap smears and colposcopy, with histopathologic results as the gold standard.

**Statistical analysis:** Data were entered checked and analyzed using Epi-Info version 6 and SPP for Windows version 8.

## Results

In this prospective controlled study, 50 patients with post contact bleeding presented to Outpatient Clinic of Obstetrics and Gynecology Department. Age was shown in Table 1, forty patients (80%) belonged to the sexually active reproductive age group, only 2 patients (4%) were below 20 years and 3 patients (6%) were postmenopausal.

Age	No	%
< 20 years	2	4
21-30 years	18	36
31-40 years	22	44
41-50 years	7	14
> 50 years	1	2
Mean ± SD		36.3 ± 10.1
Range		19-55
PARITY	No	%
Nullipara	2	4
Para 1	4	8
Para 2	17	34
Para 3	14	28
Para 4	13	26

Mean ± SD		2.2 ± 2.1
Range		0-11
Patient characteristics	No	%
<b>Occupation</b>		
Unemployed	46	92
Employed	4	8
<b>Education</b>		
Illiterate	10	20
Read and write	21	42
Moderate education	19	38
High education	0	0
<b>Residence</b>		
Rural	24	48
Urban	26	52
<b>Smoking</b>		
Yes	0	0
No	50	100
<b>Types of contraception</b>		
Oral contraception	20	40
Injected contraception	20	40
Tubal ligation	2	4
Condom	2	4
IUCD	6	12
<b>Duration of symptoms</b>		
0-3 months	23	46
4-6 months	11	22
7-9 months	2	4
10-12 months	7	14
> 12 months	7	14

**Table 1.** Demographic data of patients.

Postcontact bleeding was infrequently seen in nulliparas i.e. 2 patients (4%), primiparous in 4 patients (8%) and 44 patients (88%) were multiparas. All patients were non-smoker and non-alcoholic. None of the 50 patients was pregnant and all patients belonged to low socioeconomic status. Approximately, two thirds of the patients i.e. 34 patients (68%) reported the symptoms early i.e. within 6 months of onset and 7 patients (14%) waited for more than one year. All women had undergone cytological examination. Cytology identified 6 patients (12%) only with LGSIL and 3 patients (6%) with HGSIL. The majority of patients i.e. 34 patients (68%) had nonspecific inflammation and 6 smears (12%) had metaplasia Table 2. Colposcopically directed biopsies were obtained in total of 16 patients (32%) of all patients who had an atypical transformation zone in 15 patients (30%) and unsatisfactory colposcopy in one patient (2%) Table 3. Histological examination of obtained biopsies revealed that: Five patients (10%) had viral changes with CIN I, two patients (4%) had CIN II, one patient (2%) had CIN III and eight patients (16%) had chronic cervicitis, as shown in Table 4. AS shown in Tables 5 and 6. Colposcopy had a positive predictive value of 50% i.e. 8 of 16 patients had a positive histopathology. Sensitivity of colposcopy was 88% and specificity was 79%.

	No	%
Normal	1	2
Abnormal		
LGSIL	6	12
HGSIL	3	6
Non-specific inflammation	34	68
Metaplasia	6	12
Total	50	100

**Table 2.** Results of cytological examination.

	No	%
Typical transformation zone	34	68
Atypical transformation zone	15	30
Grade I	11	22
Grade II	3	6
Grade III	1	2
Unsatisfactory	1	2

**Table 3.** Colposcopic findings.

	No	%
Chronic cervicitis	8	16
CIN I	5	10
CIN II	2	4
CIN III	1	2

**Table 4.** Histopathological findings.

False Positive (FP)	True Positive (TP)	True Negative (TN)	False Negative (FN)
8	8	31	1

**Table 5.** Application of sensitivity and specificity tests and calculation of predictive value of positive results as regard colposcopy.

False Positive (FP)	True Positive (TP)	True Negative (TN)	False Negative (FN)
7	8	37	6

**Table 6.** Application of sensitivity and specificity tests and calculation of predictive value of positive results as regard cytology.

Cytology had a positive predictive value of 53% i.e. 8 of 15 patients had a positive histopathology. Sensitivity of cytology was 57% and its specificity was 84%.

On comparison between colposcopy and cytology:

- I. Colposcopy (88%) was more sensitive than cytology (57%).
- II. Cytology (81%) was more specific than colposcopy (79%).

Predictive values of positive results were comparable i.e. colposcopy was 50% and cytology was 53%.

## Discussion

Postcontact Bleeding (PCB) is defined as non-menstrual bleeding that occurs following sexual intercourse, vaginal examination and vaginal douches. PBC has many causes the most serious being precancerous cervical lesion. Colposcopy done for every case of PCB, the main aim of investigation of PCB is to exclude precancerous cervical lesion [4].

In this study, we used cervical cytology to evaluate women with unhealthy cervix, and colposcopy is performed to all cases. Histopathological examination is done for positive cytological and colposcopic cases. This study included 50 women. The wide range of age (mean, 36.3 years), parity (mean, 2.2), occupation, levels of education and residence of the women were included in this study making them more or less represented the general population.

This study included 50 women only who referred for cytopathology and colposcopy because there was logistic difficulty in performing cytopathology and colposcopy for all women due to the economic cost, man hours and difficulty in convincing the women. The wide range of age (mean, 36.3 years), parity (mean, 2.2), occupation, levels of education and residence of the women were included in this study making them more or less represented the general population.

Another study included 200 women (100 cases and 100 controls) with the mean age of both cases and controls was 47 years, almost all women were Muslims (97%) and about a third had been born in Bamako. They found that there was no statistical difference as regard the result of cervical lesions and age (p value=0.95) [5].

On the other hand, In other study it was found that cervical cancer in women less than 19 years of age is rare compared with older women. The highest reported prevalence (3.77%) of Squamous Intraepithelial Lesions (SIL) among 10,296 cytology smears from patients aged 10 to 19 years, 18 percent of SILs were high grade [6].

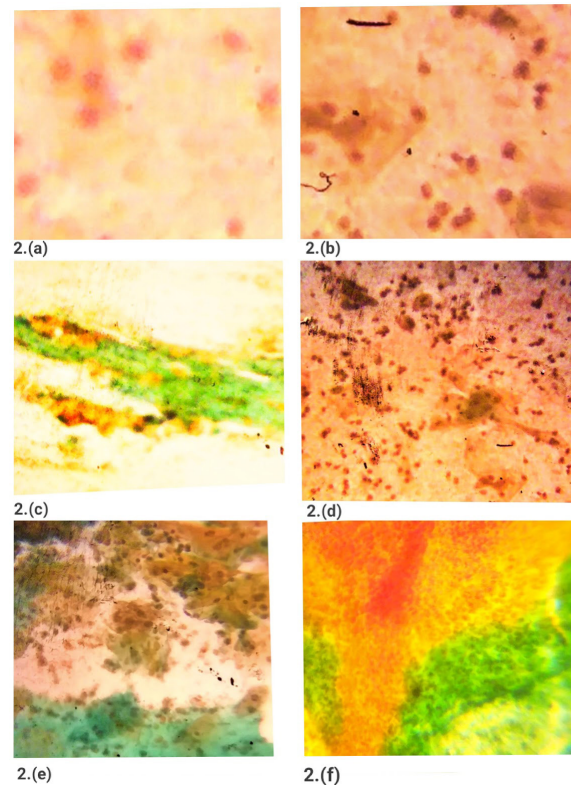
Ries et al. reported that the incidence rate of invasive cervical cancer was 0/100,000 year for ages 10 to 14 years; 0/100,000/year for ages 15 to 19 years and 1.7/100,000/year for ages 20 to 24 years from 1995 to 1999 [7].

Other study found that only three percent of adolescents with LSIL progressed to HSIL within three years. On the other hand, five percent of adolescents who developed an HPV infection developed a HSIL, half of whom did not have a preceding detectable LSIL [8].

In our study Incidence of unhealthy cervix among the 50 women did not reflect the true incidence in Egypt. Women were showing mild cytological changes. Cytology identified 6 patients only with LGSIL and 3 patients (6%). The majority of patients i.e. 34 patients (68%) had nonspecific inflammation and 6 smears (12%) had metaplasia. So, we preferred immediate referral for cytopathology and colposcopy for those patients at risk of not being treated in a timely manner, of not returning for a second appointment.

According to Jeffcoate, cervicitis is a common finding in nearly all multiparous women and in many nulliparous women as well. This could be the reason for inflammatory report in most of the Pap smear test in the study as majority of women had at least one child Figures 2a-2f.





**Figure 1.** (a):Pap smear of normal cervix( $\times 100$ ,Papnucleolar stain); 2.(b):Pap smear of ASCUS(Atypical squamous epithelial Cells of Undetermined Significance) with presence of scattered atypical cells with mildly enlarged hyperchromatic nuclei( $\times 100$ ,Pap); 2.(c):Pap smear of CIN Low grade/Grade I showing mild atypical changes with mildly irregular membrane and hyperchromatic nuclei( $\times 100$ ,Pap);

2.(d):Pap smear of CIN High grade/Grade II showing moderate atypical changes with moderate irregular membrane and hyperchromatic nuclei( $\times 100$ ,Pap); 2.(e):Pap smear of CIN High grade/Grade III showing marked atypical changes with severe irregular membrane and enlarged hyperchromatic nuclei( $\times 100$ ,Pap); 2.(f):Pap smear of Squamous cell carcinoma showing marked hypercellularity. The malignant cells arranged in sheets showed marked atypia with irregularly hyperchromatic nuclei with marked pleomorphism( $\times 100$ ,Pap).

In the present study, women who were married and had begun their sexual activity before 20 years of age were more likely to have an unhealthy cervix. Unhealthy cervix was also more common among the women with 3 or more children. Repeated childbirth may cause injury to cervix and erosion and cervicitis are also common in multipara, which can give cervix an abnormal appearance as remarked by Jeffcoate [9].

Colposcopy revealed atypical transformation zone in 15 patients (30%). Majority of patients i.e. 34 patients (68%) had typical transformation zone and only one patient (2%) had unsatisfactory colposcopic findings.

Vascular ectopy was the commonest benign lesion seen in colposcopy and it is a term coined for an erosion or ectopy surrounded by a well-vascularized, metaplastic epithelium. It was detected in 15 patients (30%).

Sensitivity of colposcopy was 88% and specificity was 79%. Sensitivity of cytology was 57% and its specificity was 84%; so, colposcopy was more sensitive and less specific than cytology in this study and previous study [10] that was done in the early cancer detection unit.

The positive predictive value of colposcopy in this study was 50%. The predictive value of positive results of cytology and colposcopy were almost comparable i.e. 53% and 50%, respectively.

In this study, false positive rate of colposcopy was 50% which was comparable to that of pap smear (46%). The false negative results of colposcopy was markedly low (3%) as compared to 13% of cytology.

Although this is time consuming and expensive in screening program, it may prove worthwhile in women with unhealthy cervix. This was designed to produce a thin layer smear from cells collected in fluid medium.

Slides prepared by this method show optimal cell preservation, minimal

overlap and reduced debris, inflammatory cells and blood, thus simplifying screening.

In this group of women with unhealthy cervix that the index of suspicion of malignancy is high, investigation work up through smears and colposcopy is mandatory in all cases.

The commonest cause of unhealthy cervix was a vascular ectopy. In the absence of neoplasia and infection, a vascular ectopy which is persistently symptomatic, may be treated by conservative measures, such as cauterization, cryotherapy or laser vaporization.

Singh, et al. commented that visual screening was inferior to cytology or colposcopy as it detected only 63% of abnormality in comparison to 71% by cytology or colposcopy and concluded that visual screening would still be useful where cytological screening is not feasible [11].

Similarly, Misra, et al. reported 11.2% cervical dysplasia and 1.9% malignancy in cytology of unhealthy cervix compared to 3.3% dysplasia and 0.02% malignancy in healthy cervix [12].

Similarly in a small study of Pap test done in 100 women, dysplasia was seen in 7 women with clinically normal looking cervix, 6 in cervicitis and one each in atrophic uterus and cervical polyp. Dysplasia occurs in majority of healthy cervixes [13].

A big study was conducted in 6 different countries with total number of women participating 56, 939 women which adds to the strength of the results. There was similar or comparable level of sensitivity and specificity to our study [14].

Other 2 studies had lower sensitivity than this study but still high indicating the good performance of the tests [15,16].

Pradhan, et al. compared cervical cytology in women with health/unhealthy cervix. They derived that dysplasia was slightly higher among the women with unhealthy cervix in comparison to healthy cervix, but the difference was not statistically significant. Hence, they emphasized on the importance of universal screening of both the healthy and unhealthy looking cervix [17].

Tehrani, et al. Evaluated women with Postcontact Bleeding (PCB) using clinical examination, cytology, colposcopy, and pathologic findings. Because of its higher sensitivity, colposcopy can be recommended for the investigation of persistent PCB, even if women with persistent PCB have a normal physical examination and negative cytologic result [18].

In our patients, fourteen patients (28%) had satisfactory re-examination. The conversion from unsatisfactory to satisfactory colposcopy was not statistically significant (p=0.2). All these patients in our study with successful conversion from an unsatisfactory to a satisfactory re-examination after they were treated by inserting vaginal misoprostol had BMI < 25 kg/m<sup>2</sup>. Ten out of fourteen patients were parous and premenopausal, and eleven out of ten patients had LSIL indication.

Three patients of the fourteen patients had side effects before the re-examination. The side effects included abdominal pain (13.3%), perception of increase in body temperature (10%) and vomiting in one patient (3.3%). Only one patient had mild abdominal pain at 2 weeks after the re-examination. There were no severe or life-threatening side effects.

The American Cancer Society reported that the overall age-adjusted incidence rates of cervical squamous cell carcinoma declined by 51%, from 13.39 per 100,000 women in 1970-1972 to 6.56 per 100,000 women in 1994-1996. Conversely, incidence rates of adenocarcinoma and adenosquamous carcinoma increased considerably, from 1.3 and 0.15 per 100,000 women respectively, in 1970-1972, to 1.83 and 0.41 per 100,000 women respectively, in 1994-1996. The observed increase in overall incidence rates of adenocarcinoma and adenosquamous carcinoma was mainly observed in women aged 20-49 years. The risk of developing such invasive carcinomas of the cervix in the 20-34 year and 35-49 age groups trebled or doubled respectively, over that period. The incidence rates of cervical adenocarcinoma for older women decreased slightly [19].

Masaad studied 2131 women with AIDS (1661 HIV-positive and 470 HIV-negative) and observed that 62.7% of the HIV-positive women and 31.7% of the HIV-negative women had evidence of HPV infection; 13.6% and 3.6%, respectively, had oncogenic HPV strains associated with cervical cancer. At baseline, 37.7% of the HIV positive women and 17.3% of the HIV negative women had abnormal cervical cytology of any grade, mostly ASCUS (19.5% and 10.8%), AGCUS (1.9% and 2.7%), or low-grade SIL (14.1% and 2.5%). High-grade SIL was seen in 32 (2.1%) of the HIV-positive and 6 (1.4%) of the HIV-negative women, while only one HIV-positive woman and no HIV-negative women had cervical carcinoma [20].

Tam, et al. Found that the rate of abnormal Pap smears in women with Systemic Lupus Erythematosus (SLE) was 16.5% compared to just 5.7% in the health population. They also found that the rate of squamous intraepithelial lesion was almost 6 times higher in lupus patients compared to those without the disease (11.8% versus 2%). So, they proved that SLE itself remained an independent risk factor for abnormal Pap smears [21].

Thanappapasr et al. Assessed the effectiveness of misoprostol in overcoming an unsatisfactory colposcopy in the patients with an abnormal cervical cytology and stated that four hundred micrograms of vaginal misoprostol were not proved to be effective in converting an unsatisfactory to a satisfactory colposcopy [22].

## Conclusion

All women at high risk for development of cervical precancerous lesions should be screened annually with special attention to women married at teenage, smokers, immunosuppressed and those with postcontact bleed. Colposcopy fills the gap between cytology and histopathology. So, we recommend the widespread use of colposcopy in all university hospitals and general hospitals to detect cervical lesions. As cytology detects a crime, the colposcopy locates the culprit. Workshops and training programs for colposcopy are also recommended.

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