**East African Scholars Journal of Medical Sciences**
*Abbreviated Key Title: East African Scholars J Med Sci*
ISSN: 2617-4421 (Print) & ISSN: 2617-7188 (Online)
Published By East African Scholars Publisher, Kenya

Volume-7 | Issue-5 | May-2024 | DOI: 10.36349/easms.2024.v07i05.009

OPEN ACCESS

**Original Research Article**

# Colposcopy Assessment of Persistent Inflammatory Changes in Cervical Cytology

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**Article History**
**Received:** 08.04.2024
**Accepted:** 15.05.2024
**Published:** 24.05.2024

**Journal homepage:**
https://www.easpublisher.com

**Quick Response Code**

**Abstract:** ***Introduction:*** It has been reported that inflammation on Pap smear is quite common. Chronic inflammation, whether specific or nonspecific, has been linked to cancer development and is considered one of the factors responsible for carcinogenesis. Women who have persistent inflammation on Pap smear should undergo further evaluation and treatment. ***Objective:*** This research aims to study the effectiveness of colposcopy in terms of assessing persistent inflammatory changes in cervical cytology e.g., Pap smear. ***Methods:*** Between January 2021 and January 2024, this prospective study was carried out in the Department of Obstetrics and Gynecology at Holy Family Red Crescent Medical College Hospital in Dhaka, Bangladesh. The study involved screening 320 women with Pap smear tests. Women who received an inflammatory Pap smear report, aged between 20 years and 65 years, were included in the study. Both partners were treated and advised to use barrier contraception for the same duration. These women were asked to come back after six weeks for Pap smear and VIA follow-up tests. Patients with persistent inflammation, even if VIA negative, were then referred for colposcopy and guided biopsy. ***Results:*** Out of a group of 320 women, 234 (73.13%) had an initial Pap smear report suggesting inflammation. Out of all the women who were examined, 21% had normal colposcopic findings while 79% had abnormal findings. After a histopathological examination (HPE), it was found that 69% of women had cervical intraepithelial neoplasia (CIN) 1, 23% had CIN II, 6% had CIN III, and 3% had SCC. Additionally, 25% of women tested positive for HPV DNA and 75% of women tested negative for HPV DNA. ***Conclusion:*** It is important to repeat an inflammatory smear test because persistent inflammation can cause dysplasia. Patients with persistent inflammatory Pap smears despite undergoing treatment show changes on Colposcopic directed biopsies. In addition to a Pap smear, VIA (Visual Inspection with Acetic Acid) can also be considered for follow-up.

**Keywords:** Cervical cytology, Pap smear, inflammation, smear, CIN.



## INTRODUCTION

The Pap smear is a common test used to screen for precancerous lesions in the cervix. It detects abnormal cells in the cervical lining that may indicate early stages of cervical cancer. Treatment at this stage can prevent the cancer from becoming invasive. Studies have reported a high incidence of inflammation on Pap smears [1-4]. Recent studies in our neighboring country India have reported a similarly high prevalence of inflammation on Pap smear to be 30%–40% [5, 6]. Persistent inflammation, whether specific or nonspecific, has been shown to be linked with the development of cancer and is believed to be one of the contributing factors to carcinogenesis. When there is a persistent microbial infection in and around the epithelial cells, it leads to a chronic inflammatory state, which can cause an increased rate of cellular turnover. This can result in metaplastic and dysplastic changes that may eventually progress to neoplasia. This phenomenon is thought to be caused by cytokine and free radical-mediated damages, which can cause reactive cellular hyperproliferation, leading to further mutations [7]. Persistent inflammation on Pap smear can lead to the missing of cervical

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premalignant changes due to the low sensitivity and high false-negative rate of the test. Therefore, women with such inflammation should undergo further evaluation and treatment. However, the management of women with persistent inflammatory changes without atypia is not clear yet as the association between dysplastic changes and cervical intraepithelial lesions (cervical intraepithelial neoplasia [CIN]) varies. In such cases, the cervical screening algorithm recommends treating the infection and repeating the Pap smear after 4–6 weeks [8-11]. If a Pap smear shows persistent inflammation, it is recommended to undergo a colposcopy. However, since inflammation is a common occurrence on Pap smears, it may not be feasible to subject all women with persistent inflammation to a colposcopy. An alternative and more affordable method of evaluation could be visual inspection after acetic acid application (VIA) [21]. Cervical cancer is most commonly associated with group of cervical lesions, mostly chronic, which include chronic cervicitis, endocervicitis, cervical erosions lacerations, polyps and leukoplakia. Early cervical epithelial changes can be identified by a Papanicolaou (Pap) smear test, which is the primary screening test for the detection of precancerous cervical intraepithelial neoplasia and the early stage of invasive cervical cancer. These changes can also be confirmed by cytology and colposcopy methods as precancerous lesions [22]. The objective of this study is to find the efficacy of colposcopy in the management of persistent inflammatory changes in cervical cytology. Ethical clearance and informed consent were taken from the respective authority.

**Objectives**

- ***General objective:*** The objective of this research is to study the effectiveness of colposcopy in the management of persistent inflammatory changes in cervical cytology.
- ***Specific objective*****:** This study aims to compare the efficacy of colposcopy and Pap smear in women with persistent inflammatory smear.

# METHODOLOGY

This cross-sectional study was conducted between January 2021 and January 2024. A total of 350 sexually active women aged between 20 years to 65 years, who visited the Department of Obstetrics and Gynecology, Holy Family Red Crescent Medical College Hospital, Dhaka, Bangladesh were part of this study. Out of 320 women screened, 234 (73.13%) had an initial Pap smear report suggesting inflammation. After a second Pap smear evaluation, 148 women were found to have persistent inflammatory smears.

- ***Inclusion criteria:*** Patients who are over 20 years of age and sexually active asymptomatic up to 65 years of age were eligible to participate in the trial. Also, women with a Pap smear report suggestive of inflammation (minimal/mild/moderate/severe) were included in the study if they provided written informed consent and understood the details of the study.
- ***Exclusion criteria*****:** Women who were excluded from the study, those with active cervical infection, vaginitis, pelvic inflammatory disease, frank malignant lesion on the cervix, current pregnancy, intrauterine contraceptive device use, history of CIN and treatment, multiple sexual partners, or history of diabetes

A group of women underwent a general physical examination, followed by a conventional Pap test. Those with persistent inflammatory Pap smear results then underwent a colposcopic directed biopsy with HPV DNA testing. The biopsies were sent for histopathological examination (HPE). For the purpose of statistical analysis, a Swede score of 0-4 as normal colposcopic findings and 5-6 and 7-10 as abnormal colposcopic findings were considered. Individual data was recorded on a pre-structured proforma for future analysis. To analyze the data, means and standard deviations of the measurements per group were used, with statistical analysis conducted using SPSS 22.00 for Windows. The difference between the two groups was determined using the chi-square test, with a significance level set at $p<0.05$ The ethical review committee of Holy Family Red Crescent Medical College Hospital has approved the study. A well-informed written consent paper was signed by the patients.

# RESULT

More than 350 women were interviewed and selected primarily for the study. Among them, 5 women conceived during the study period and 7 crossed 65 years. 18 of the selected patients stopped visiting which caused data loss [Figure-1]. The study patients were of mean age 49.32±10.62 years, multipara 85% and the mean marriage age was 21.30±4.02 years [Table 1]. The majority of women complained of pain in the abdomen (25%). The second most common complaint was of white discharge per vaginum (21%). 16% of women presented with menorrhagia, and 12% had irregular cycles. Additionally, 13% of women presented with urinary tract infections (UTIs), while 14% were asymptomatic [Table 2]. Out of 234 patients, 21% had normal colposcopic findings and 79% had abnormal colposcopic findings. Among abnormal colposcopic findings 55% belong to the Swede score of 5-6 and 25% belong to the Swede score of 7- 10 [Table 3]. Among the women with positive findings on histopathology suggestive 69% of women had CIN 1, 23% had CIN II, 6% had CIN III and 3% had SCC [Table 4]. Out of 234 women, 48 women had normal colposcopic findings. Among normal colposcopic findings, 48 women were found to have CIN 1 on HPE [Table 5]. Out of 234 women, 186 had abnormal colposcopic findings. Of those with abnormal findings, 118 were diagnosed with

CIN I on HPE, 54 had CIN II on HPE, 12 had CIN III on HPE, and 6 had SCC on HPE [Table 6].

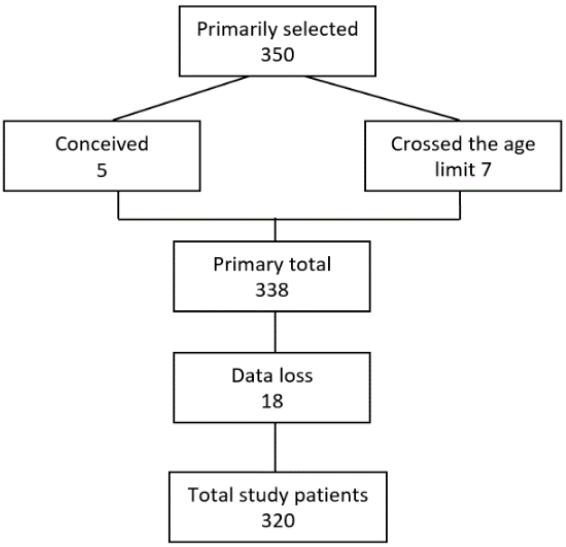


**Figure-1: Total patient selection**

**Table-1: General characteristics of the study sample**

| Parameters | Range |
|---|---|
| Mean age (years) | 49.32±10.62 |
| Multipara (%) | 199 (85%) |
| Age of marriage | 21.30±4.02 |

**Table-2: Distribution of study patients according to clinical presentation**

| Histopathology | N (%) |
|---|---|
| Asymptomatic | 33 (14%) |
| Pain abdomen | 57 (24%) |
| Menorrhagia | 39 (16%) |
| Irregular cycles | 27 (12%) |
| White discharge per vaginum | 48 (21%) |
| Urinary tract infection | 30 (13%) |

**Table-3: Distribution of study patients according to their colposcopy findings (Swede score**

| Score | N (%) |
|---|---|
| 0-4 | 48 (21%) |
| 5-6 | 129 (55%) |
| 7-10 | 57 (24%) |

**Table-4: Histopathology Findings**

| HPE findings | N (%) |
|---|---|
| CIN I | 162 (69%) |
| CIN II | 54 (23%) |
| CIN III | 12 (5%) |
| SCC | 6 (3%) |

**Table-5: Correlation between normal colposcopy findings with HPE**

| HPE findings | N | Normal findings (N=48) |
|---|---|---|
| CIN I | 207 | 48 |
| CIN II | 54 | 0 |
| CIN III | 12 | 0 |
| SCC | 6 | 0 |

**Table-6: Correlation between abnormal colposcopy findings with HPE**

| HPE findings | N | Abnormal findings (N=186) |
|---|---|---|
| CIN I | 207 | 114 |
| CIN II | 54 | 162 |
| CIN III | 12 | 12 |
| SCC | 6 | 6 |

# DISCUSSION

The Pap smear test has been found to be effective in screening for cervical cancer on a large scale. This test has resulted in a significant reduction in cervical cancer mortality due to the relatively long pre-invasive phase of the disease. It is easy to examine the uterine cervix for abnormalities, and the technology used to process the cervical smear is readily available [12-14]. A concern among clinicians regarding persistent inflammatory smear has arisen as it causes a cellular microenvironment of chronic inflammation which predisposes to metaplastic and dysplastic changes in the cervical epithelium [7].

Proper and accurate guidelines for the management of inflammatory smears are scanty [8-11]. Generally, the protocol is to treat the woman with antibiotics with a repetition of the smear after 4–6 weeks. This conservative approach causes regression of inflammation in the majority of the cases.

According to a study conducted by Brown and Phillips, CIN 3 was found in 30% of cases where persistent inflammation was detected on Pap smear [15]. The current study revealed that 73.13% of women with persistent inflammation on Pap had various grades of CIN. This highlights the importance of following up on inflammatory smears as per the institution's protocol to avoid missing any cases of pre-invasive and invasive cervical cancer. Only one inflammatory Pap smear should concern the clinician or not, was studied to find the incidence of dysplasia in a single inflammatory smear [16]. A total of 514 women underwent Pap smears in this study, out of which 414 were found to have inflammatory changes. These women underwent colposcopy and biopsy, and the results showed that 11 cases of intraepithelial neoplasia were detected. It's important to note that this study only evaluated the result of single smear reports and did not take into account any changes that may have occurred after antibiotic use through colposcopy.

As part of a study [17], researchers evaluated the effectiveness of Pap smear after a brief course of antibiotics. They repeated the smear after 3 months and found that inflammation on Pap smear persisted in 79% of cases, regressed in 12% of cases, and progressed to CIN in 8% of cases. In our study, 33.75% of participants had persistent inflammation, while 52.5% showed regression. The researchers concluded that it was not possible to implicate a specific organism as the cause of inflammation, and therefore, adequate treatment was not possible. The inflammation could either be a result of underlying viral infection or reactive changes in the mucosa. A study was conducted on a large population [18] to investigate the use of two smears taken 10-12 weeks apart. The first inflammatory smear was treated with a course of antibiotics, while the second inflammatory smear was followed up with colposcopy and guided biopsy. The aim of the study was to determine the incidence of a premalignant lesion in the background of inflammation of the cervix despite treatment. The study found that 14.2% of women had persistent inflammatory smears, and 22.7% had dysplasia. One-fifth of women with inflammation alone had underlying dysplasia, which indicated that persistent inflammatory cellular changes should not be considered a normal variant. These changes require further investigation, especially when they persist following adequate therapy. The present study found that 73.13% of women had persistent inflammation and 79% had CIN.

A study conducted by Bhutia *et al.*, [19] in the Indian subcontinent involved 420 women, where an inflammatory smear was followed up with a course of antibiotics lasting 8-14 days. A second smear was taken after 6-12 weeks, and the rate of inflammatory smear was reported to be 24.3%, with 8.6% showing persistent inflammation. Women with persistent inflammation on the second smear underwent colposcopy and guided biopsy. Among them, 30 women (16.67%) were diagnosed with CIN. Dasari *et al.*, [20] conducted a study on 150 women and found that 20.9% of them had premalignant lesions. In cases where inflammation persisted, a colposcopy and guided biopsy were performed. The first report of inflammation was followed with a course of antibiotics for 7-14 days and a repeat smear was taken after 2 weeks. The study also showed that CIN 2/3 and carcinoma in situ together contributed to 6.9% of the cases.

A study conducted by Garg and Deasi found that out of all symptomatic women, 21% had normal colposcopic findings. On the other hand, 38.5% had abnormal colposcopy, 28.5% had miscellaneous findings, and 12% had indecisive colposcopic findings [22]. Another study by Manjula revealed that colposcopic diagnosis was inflammatory in 27 (54%) cases, followed by cervical intraepithelial neoplasia (CIN) 1 in 12 (24%) patients [23].

**Limitations**

This was a single-centre study with a large population for a longer period of time. These may cause

data loss and not provide the overall scenario of the county.

## CONCLUSION

In the current study, colposcopy has been proven to be a good option for the follow-up of persistent cervical inflammation. Considering the poor rate of follow-up and the logistical restrictions in repeating Pap smear, VIA can also be considered as a follow-up method, as it is cheap, easily available, and reproducible, especially in low-resource settings.

**Funding:** Self-funded research.

**Conflicts of interest**: N/A

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**Cite This Article:** Ayesha Nigar Nur, Meherun Nessa, Ferdousi Begum (2024). Colposcopy Assessment of Persistent Inflammatory Changes in Cervical Cytology. *East African Scholars J Med Sci*, *7*(5), 220-224.