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**Original Research Article**

# Screening of HIV sero positive women for cervical abnormalities

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## ABSTRACT

**Background:** Cancer cervix is a leading cause of death among women worldwide. Detection of cervical cancer in precancerous stage is 100% curable. Screening with Pap smear has reduced mortality by cervical cancer in developed countries many folds. The objective of the study is to determine prevalence of Cervical Intraepithelial Neoplasia (CIN) in HIV infected women and observe for associated lower genital infections and their correlation with CD4 counts.
**Methods:** The present study is a cross-sectional observational study conducted at PGIMS, Rohtak, Haryana for a period of 18 months. 150 HIV patients and 150 age related control cases were taken. Pap smears were taken and analyzed for cervical abnormalities and genital infections.
**Results:** Of the 300 Pap smear 22 (7.3%) has squamous intraepithelial abnormalities and 278 (92.7%) negative for intra epithelial abnormalities. Prevalence of cervical intraepithelial abnormities among HIV positive 12% while among HIV negative it is 2.7%. Cervical intraepithelial abnormalities were found in 40% and 3.5% of patients with CD4 count <200 and >200 respectively.
**Conclusions:** HIV increases the risk of cervical abnormalities. Frequent screening of these patients for cervical cancer is needed.

**Keywords:** HIV, Pap smears screening, Squamous intraepithelial lesion

## INTRODUCTION

Cervical cancer is a leading cause of death among women worldwide. Cervical screening has reduced the incidence of cancer cervix in many advance countries.[1,2] It has got a long pre-invasive state which could be detected and treated. So, screening is highly effective.

Cervical Intraepithelial Neoplasia (CIN) arises in an area of metaplasia in the transformation zone at the advancing squamo-columnar junction in most cases. CIN is most likely seen at menarche and after pregnancy when metaplasia is most active. Detection of cervical cancer in precancerous stage is 100% curable. Screening with Pap smear has reduced mortality by cervical cancer in developed countries many-folds. Association of cervical intraepithelial neoplasia and HPV infection approaches 90%.[3] Incidence, prevalence and persistence of HPV with high risk subtype are more common with HIV infection and worsen with immuno-suppression like increased CD4 cell count and increased viral load.[4] India faces large burden of HIV/AIDS (third highest number in world).

Authors have evaluated the HIV positive patients, attending Out Patient Department of Obstetrics and Gynecology at Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana to establish the relationship between cervico-vaginal cytological abnormalities, state of HIV infection and CD4 count.

The objective of the study is to determine prevalence of Cervical Intraepithelial Neoplasia (CIN) in HIV infected

women and observe for associated lower genital infections and their correlation with CD4 counts.

## METHODS

The present study was conducted in the out-patient Department of Obstetrics and Gynecology and pathology of Pt. B.D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana. A total of 150 HIV positive patients and 150 age matched control cases were taken.

### *Inclusion criteria*

- Both HIV seropositive type1 and 2 women attending ART clinic with age group18-45 years
- Patients sero-positivity tested by ELISA test and confirm by western blot test.

### *Exclusion criteria*

- Pregnant women
- All diagnosed cervical cancer whether invasive or pre-invasive.

After an informed consent all women were interviewed regarding their social, obstetric, sexual, medical and treatment history. General physical, pelvic examination and cervico-vaginal, Pap smear of all enrolled women were done. Universal precautions were taken while collecting samples. Blood samples were taken to determine CD4 count. Cytological changes and genital infections were observed and compared between sero-positive and sero-negative cases.

### *Statistical analysis*

Statistical analysis was performed using IBM SPSS statistics (SPSS/IBM chicagoIL). The results were interpreted using Chi-square method.

## RESULTS

The present study is a cross-sectional observational study conducted for a period of 18 months. Results are tabulated from 1-6.

A total of 150 HIV positive and 150 control cases were taken.

Table 1 shows demographic profile of patients. All the women in present study were in reproductive age group of 19-45 years. Majority of women in present study were in the age group of 21-30 years followed by 31-40 years. Both the groups had comparable data in terms of age (independent samples t-test p>0.05). Majority of women in both groups were multiparous and were comparable.

Nearly 51% women had their first intercourse before the age of 18 while 49% had after it. Only 2.6% (8/300) had sex before the age of 15. Each one of them had sex with single partner only (Table 2).

**Table 1: Demographic profile of patients.**

| Age in years | HIV-negative | HIV-positive | Total |
|---|---|---|---|
| <20 | 2 (1.3%) | 3 (2%) | 5 |
| 21-30 | 76 (50.6%) | 73(48.6%) | 149 |
| 31-40 | 59 (39.9%) | 65(43.3%) | 124 |
| >40 | 13 (8.7%) | 9 (6%) | 22 |
| Mean±SD | 31.7±6.8 | 31.2±6.1 | |
| p-value* | 0.47 | | |
| **Parity** | | | |
| 0 | 1 | 6 | 7 |
| 1-3 | 126 | 123 | 249 |
| >3 | 23 | 21 | 44 |
| Total | 150 | 150 | 300 |

*independent samples test

43% HIV positive women had their CD4 counts>350 cells/µl while 23% were severely immune-compromised with CD4 count of <200 cells/µl .33% had CD4 counts between 200-350/l (Table 3).

**Table 2: Distribution according to age at first intercourse.**

| Age (years) | HIV-negative | HIV-positive | Total |
|---|---|---|---|
| <18 | 70 (46.7%) | 84 (56.0%) | 154 (51.3%) |
| >18 | 80 (53.3%) | 66 (44%) | 146 (48.7%) |
| Total | 150 | 150 | 300 |

**Table 3: Distribution of HIV positive women according to CD4 counts.**

| CD4 counts (cell/µl) | No. of patients | Percentage |
|---|---|---|
| <200 | 35 | 23.3 |
| 200-350 | 50 | 33.3 |
| >350 | 65 | 43.3 |
| Total | 150 | 100 |

**Table 4: Distribution of epithelial abnormalities according to HIV status.**

| Epithelial abnormalities | HIV positive | HIV negative | Total |
|---|---|---|---|
| ATYPIA+ | 18 (12%) | 4 (2.7%) | 22 (7.3%) |
| ATYPIA- | 132 (88%) | 146 (97.3%) | 278 (92.7%) |
| Total | 150 | 150 | 300 |

OR 18.5* ,95 CI (5.5-61.7) p=0.002; *Chi-square test

Of the 300-pap smear, 278 (92.7%) reported negative for intra-epithelial lesion and 22 (7.3%) had squamous cell abnormalities. The prevalence of squamous cell abnormalities among HIV +ve was 12% (18/150) while among HIV -ve women it was 2.7% (4/150) a statistically

significant difference (OR 18.5, 95%CI (5.5-61.7) p=0.002) (Table 4).

Cervical epithelial abnormalities were found in 40% and 3.5% of patients with CD4 count <200 and >200 respectively (OR 18.5, 95% CI (5.5-61.7) P<0.00). Thus, in present study incidence of cervical atypia increased with falling CD4 counts (Table 5).

**Table 5: Frequency distribution of epithelial cell abnormalities according to CD4 counts in HIV patients.**

| CD4 counts | ATYPIA+ | ATYPIA- |
|---|---|---|
| <200 (n=35) | 14 (40%) | 21 (60%) |
| >200 (n=115) | 4 (3.5%) | 111 (96.5%) |
| Total | 18 | 132 |

OR 18.5* ,95 CI (5.5-61.7) p<0.001; *Chi-square test

Vaginal infections were found in 19.3% and 4.7% of cases and controls (OR 4.90, CI 2.07-11.57). Thus, HIV positive status was significantly associated with vaginal infections (Table 6).

**Table 6: Distribution of infection according to HIV status.**

| | HIV positive | HIV negative | Total |
|---|---|---|---|
| Infection+ | 29 (19.3%) | 7 (4.7%) | 36 (12%) |
| Infection- | 121 (80.7%) | 143 (95.3%) | 264 (88%) |
| Total | 150 | 150 | 300 |

OR 4.90*,95%CI (2.07-11.57) p<0.001; *Chi-square test

## DISCUSSION

Carcinoma cervix remains a major cause of morbidity and mortality among women, especially in developing world, where routine cytological screening is generally unavailable. Squamous intraepithelial lesions (SILs) of the uterine cervix are among the most prevalent gynecological manifestations of HIV infection. In the present study, cytopathological changes and evidences of infection were detected in Pap smear of HIV patients and control were correlated with CD4 counts. All the patients in present study were in reproductive age group (19-45 years). Maximum number of cases (48.6%) and controls (50.6%) were in the age group of 21-30 years followed by 31-40 years. Mean age in HIV+ve group was 31.2±6.4 years while in HIV-ve it was 31.7±6.8 years which was almost similar to study of Hawes et al in which the mean age was 31.0 years among the cases and 31.9 years among the controls.[5]

Nearly 51% women had their first intercourse before the age of 18 years in our study. All the women had relation with single partner only while the study by Schuman et al revealed that more than 30% women had multiple sexual partners.[6] Discordance can be explained by reluctant behavior of studied patients in disclosing their sexual lives and prevalence of monogamous relationship in our culture.

In the present study, the prevalence of cervical squamous abnormalities among HIV +ve was 12% (18/150) while among HIV-ve it was 2.7% (4/150), which has statistically significant difference (OR 18.5, 95% CI (5.5-61.7) p=0.002). In the study of Devi et al prevalence of abnormal Pap smear was 7.17% in HIV positive women as compare to normal while the study of Micheletti et al observed increase incidence of squamous intraepithelial lesion (SIL) 22.2% versus 5.9% in HIV+ve and HIV-ve respectively.[7,8] In the present study comparative lower incidence of Pap smear abnormalities could be explained because of comparative lesser high risk behavior including intravenous drug abuse, multiple sexual partners and absence of HIV-2 in present study group. In the present study cervical intraepithelial abnormalities increased with progression of disease and increasing immuno-suppression with falling CD4 counts (40% when CD4 counts <200 and 3.5% when counts >200) while Six et al observed 7.5% prevalence for SIL for HIV- ve and 31.3% for HIV+ve women with CD4 count less than 500 in their study.[9] In a cross sectional study done at Brazil by Chartuni et al they observed 23% prevalence of cervical intraepithelial neoplasia in HIV positive women and more with decrease CD4 cell counts (90% occurrence when count was less than 200).[10] In present study 46% women with CD4 count <200cells/µl had vaginal infection while only 11.3% of those with CD4 count >200 cells/µl had vaginal infections which is statistically significant difference. Almost similar observation was seen in the study of Greenblatt et al (13%, 15%, 18% in women with CD4 counts >499, 200-499 and 200 cells/µl respectively).[11]

The prevalence of vaginal infection was 19.3% in HIV +ve women in present study including Gardenella vaginalis (8%), Candida albicans (5.3%), Trichomonas vaginalis (4%) and Human papilloma virus (2%). While in HIV-ve only 4.7% had vaginal infections. Similar results were observed in the study of Greenblatt et al, who found that women with HIV infection had candidiasis 15.5% versus 9% and bacterial vaginosis 18% versus 14% in HIV-ve, but no trichomoniasis whereas Warren et al observed bacterial vaginosis more prevalent in HIV +ve (47%) as compared to HIV –ve (44%) in their study.[11,12]

## CONCLUSION

It is concluded that HIV increases the risk of cervical atypia and vaginal infections. Greater frequency was associated with degree of immune-suppression which was detected by CD4 counts. Hence HIV infected women need regular and more frequent gynaecological monitoring and cervical cancer screening.

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