

Original Research Article

A Study on Cervical Pap Smear Examination in Women Living With HIV Infection

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ABSTRACT

Introduction: HIV infected women have a higher risk of HPV infection associated cervical intraepithelial neoplasia. Cancer of cervix is preventable condition if detected and treated in pre invasive stage. Pap smear examination is a simple, cheap, safe diagnostic tool for early detection of abnormal cervical epitheliums.

This study is planned to determine the prevalence and patterns of abnormal cervical smears and to correlate it with some socio-demographic factors, in HIV positive females.

Material and methods: This prospective cross sectional study was conducted from 1st August 2017 to 30th September 2017 at Government Medical College and Hospital Akola.

Total 187 HIV positive women attending the ICTC center for treatment of ART were considered for the study. Information about age, marital status, age at marriage, parity and socioeconomic status, history of STD and about ART of the participants was obtained as per the pre tested semi structured questionnaire. All participants were investigated for CD4 count and Pap smears were collected from these women. Laboratory results were reported according to the Bethesda System for Reporting Cervical Cytology.

The data so collected was analyzed by Epi Info version 7.0.

Results: Mean age of the participants was 36.9 years. The youngest participants were 19 years old while oldest was 55 years. 80.2% had NILM while 17.7 % had ASCUS and 2.1 % had LSIL.

Cervical epithelial cell abnormalities found to be more in participants having age above 50 years (64.71%), in widow/divorced group (21.84%), in women who married before 20 years of age (22.4%). in women belonging to Lower, Lower Middle or Middle class (22.4%), in participants with parity more than two (21.1%).

48.1% women with CD4 count less than 400, 32.5% females having history of STDs and 31.4% females showing less than 90% adherence to ART showed abnormal Pap smear.

Keywords: HIV, NILM, ASCUS, LSIL, CD4 count, Pap smear

INTRODUCTION

Cervical cancer and infection with Human Immunodeficiency Virus are both important public health problems in developing countries. Several risk factors have been linked to cervical dysplasia and

cancer of cervix. [1-5] Among these factors, Human papilloma virus infection is the known major etiologic agent for the causation of cervical cancer. [4,5-8] Women infected with HIV have a higher risk of Human papilloma virus infection associated

cervical intraepithelial neoplasia as compared to HIV uninfected women. [9-12,7]

It has been observed that women who are immune compromised are at increased risk of having persistent HPV infection. [13] HIV is the leading cause of immune suppression worldwide and as such women with HIV are 4-5 times more likely to be infected with HPV than seronegative controls. [14,15] Women infected with HPV thus are at greater risk of developing cervical intraepithelial neoplasms and invasive cervical cancers. [16,17]

Invasive cancer of cervix is considered to be a preventable condition, given that it is associated with a long pre invasive stage, making it amenable to screening and treatment as long as it is detected early and managed effectively. [18,19] Pap smear examination is a simple, cheap, safe diagnostic tool for early detection of cervical cancer i.e. to detect the presence of abnormal atypical cells. [16]

However increasing number of women are being linked to antiretroviral therapy treatment program which have the potential to improve their lifespan long enough for cervical cancer. [16]

This study is carried out to determine the prevalence and patterns of abnormal cervical smears and to correlate it with some socio-demographic factors, in HIV positive females registered and attending antiretroviral treatment (ART) clinic at Government Medical College and Hospital, Akola.

MATERIAL AND METHODS

This was a prospective cross sectional study conducted from 1st August 2017 to 30th September 2017 at Government Medical College and Hospital Akola.

The study population comprised all HIV positive women 18 to 70 years of age who had been or were sexually active and were attending the ICTC for ART and consented to participants in the study. Pregnant and post natal mother, women who have undergone hysterectomy (as they are at the lowest risk), On their menses on the day

of collection of Pap smear, and not giving consent for Pap smear were excluded from the study. Thus During the study period, total 187 HIV positive women attending the ICTC center for treatment of ART were considered for the study. The eligible females as per the above criteria are selected when they come to the ART clinic for collection of their Antiretroviral Therapy pills.

A written consent was obtained from each study participant after providing details of the study through patient information sheet. After obtaining ethical approval from ethical committee of the institute, the study is undertaken in collaboration with Gynaecology department, ART center and Pathology department in the department of community Medicine of Government Medical College Akola. A detailed information of the participants including age, marital status, age at marriage, parity and socioeconomic status (By B.G. Prasad Scale) of the participants was obtained as per the pre tested semi structured questionnaire. Information was also obtained from participants about history of sexually transmitted diseases and about the ART (whether taking or not taking ART).

All participants are investigated for CD4 count. Cervical smear were collected from these women for Pap smear. In lithotomy position with a sterile disposable appropriate size Cusco's speculum was passed per vagina to explore the cervix. The cervix was inspected for any lesion. An Aylesbury spatula was then used to collect smear from the endocervical canal of the cervix and ectocervix. The cells obtained were immediately smeared on a pre labelled glass slide and fixed in 95% ethanol. The smear was fixed in 95% ethanol for at least 15 minutes before further processing was done in the department of pathology.

Laboratory results were reported according to the Bethesda System for Reporting Cervical Cytology. Those who had positive smear were referred for colposcopy examination and further treatment.

Statistical Analysis Of Data:

The data so collected was analyzed by Epi Info version 7.0 software of CDC. For categorical variables proportions and

mean were calculated. Chi square test was applied to find the significance of difference wherever required.

RESULTS

Table 1: Socio-demographic factors of the HIV positive women as per cervical Pap smear findings

Socio demographic factors	Cervical Pap smear findings			Total (%)
	NILM (%)	ASCUS (%)	LSIL (%)	
Age group 18-49 years	138(90.2)	11 (7.2)	4 (2.6)	153 (100.0)
>50	12 (35.3)	22 (64.7)	0 (00.0)	34 (100.0)
Marital Status Married	67(80.7)	14 (16.9)	2 (2.4)	83 (100.0)
Widow /divorced	83 (79.9)	19 (18.2)	2(1.9)	104 (100.0)
Age at marriage <20	77(73.3)	25(23.8)	3(2.9)	105(100.0)
>20	73 (89.0.)	8(9.8)	1(1.2)	82(100.0)
S-E Status Lower	31(72.1)	12(27.9)	0(00.0)	43(100.0)
Lower middle	20(60.6)	13(39.4)	0(00.0)	33(100.0)
Middle	47(88.6)	3(5.7)	3(5.7)	53(100.0)
Upper middle	38(88.4)	4(9.3)	1(2.3)	43(100.0)
Upper	14(93.3)	1(6.7)	0(00.0)	15(100.0)
Parity Nulliparous	4 (100.0)	0(00.0)	0(00.0)	4 (100.0)
Parity 1	35 (74.5)	11 (23.4)	1 (2.1)	47 (100.0)
Parity 2	51 (85.0)	6 (10.0)	3 (5.0)	60 (100.0)
Parity >2	60 (78.9)	16 (21.1)	0 (00.0)	76 (100.0)

Total 187 HIV positive women participated in the present study. The mean age of the participants was 36.9 years. The youngest participants were 19 years old while oldest was 55 years. Majority of the participants i.e. 153 (81.8%) was in the age group of 18 to 49 i.e. in reproductive age group while 34 (18.2) were above 49 years of age. 83 (44.4%) were married while 104 (55.6%) were divorced or widowed. 43(22.9%) participants belonged to lower class, 33 (17.6%) to lower middle class, 53(28.4%) to middle class, 43 (22.9%) to upper middle class and 15 (8.2%) to upper middle class. There were only 4(2.1%) nulliparous women in the study while 47 (25.1%) were para 1, 60 (32.1%) were para 2 and 76 (40.7%) were para 3 and above. Age at marriage in 125 (66.8%) participants was below 20 years, the lowest age was 16 years while in 55 (29.4%) participants it was 20 to 25 years and in 7 (3.8 %) participants it was above 25 years.

Out of 187 subjects 150 (80.2%) had NILM (Non intraepithelial lesion or malignancy) while 33 (17.7 %) had ASCUS (Atypical squamous cell undetermined significance) and 4 (2.1 %) had LSIL (Low grade squamous intraepithelial lesion). ASCUS and LSIL are at risk of

development of carcinoma cervix. Thus in the present study 37 (19.8%) subjects are at risk of cervical cancer.

Pap smear was found to be abnormal in 15 (9.81%) participants in the age group below 50 years while it was found abnormal in 22 (64.71%) participants having age above 50 years. This difference is statistically significant ($\chi^2 = 52.83, df=1, p < 0.05$)

In Married females there were 14(7.49%) females with Atypical squamous intraepithelial lesion-undetermined significance and 2 (1.07%) with Low grade squamous intraepithelial lesion while 67(36.82%) had Non-intraepithelial lesion or malignancy. In Widow/Divorced there were 19 (10.16%) females with Atypical squamous intraepithelial lesion-undetermined significance and 2(1.07%) females with Low grade squamous intraepithelial lesion while 83 (44.38%) with Non-intraepithelial lesion or malignancy according to Bethesda system.

Thus in Married HIV positive women abnormal Pap smear was found in 16 (19.28%) subjects while in widow/divorced group 21 (21.84%) subjects were having abnormal Pap smear.

In those who married below 20 years of age there were 25 (23.8%) females with Atypical squamous intraepithelial lesion-undetermined significance, 3 (2.9%) females with Low grade squamous intraepithelial lesion and 77 (73.3%) with Non-intraepithelial lesion or malignancy. Those who married after 20 years of age there were 8 (9.8%) females with Atypical squamous intraepithelial lesion-undetermined significance, 1(1.2%) females with Low grade squamous intraepithelial lesion and 73 (89.0%) with Non-intraepithelial lesion or malignancy according to Bethesda system. Abnormal Pap smear was found in 28 (22.4%) women who married below 20 years of age while it was found in 9 (14.5%) women who married after 20 years of age. Here age at marriage is statistically significant with Pap smear findings i.e. risk of development of cervical cancer depends upon Age at Marriage of female. Chi Square=7.14,df=1 p-value <0.05.

In HIV positive women who belongs to Lower or Lower Middle or Middle class, there were 28 (20.4%) females with Atypical squamous intraepithelial lesion-undetermined significance, 3 (2.2%) females with Low grade squamous intraepithelial lesion and 106 (77.4%) with Non-intraepithelial lesion or malignancy. In Participants belonging to Upper middle or Upper class there were 5 (10.0%) females with Atypical squamous intraepithelial lesion-undetermined significance, 1(2.0%)

females with Low grade squamous intraepithelial lesion and 44 (88.0%) with Non-intraepithelial lesion or malignancy.

Abnormal Pap smear (ASCUS + LSIL) was found in 31(22.4%) cases in Lower or Lower Middle or Middle class while it was found in 6 (10.3%) cases belonging to Upper middle or Upper class.

Socioeconomic status is statistically significant with Pap smear findings i.e. risk of development of cervical cancer depends upon Socio economic status of female in this study. Chi Square=4.72, df=4, p-value <0.05.

In Nulliparous there were no females with atypical squamous intraepithelial lesion-undetermined significance or females with Low grade squamous intraepithelial lesion. In Para 1 there were 11 (23.4%) females with Atypical squamous intraepithelial lesion-undetermined significance, 1 (2.1%) female with Low grade squamous intraepithelial lesion and 35 (74.5%) with Non-intraepithelial lesion or malignancy. In Para 2 there were 6 (10.0%) females with Atypical squamous intraepithelial lesion-undetermined significance, 3 (5.0%) females with Low grade squamous intraepithelial lesion and 51 (85.0%) with Non-intraepithelial lesion or malignancy. In Para ≥ 3 there were 16 (21.1%) females with Atypical squamous intraepithelial lesion-undetermined significance while there were 60 (78.9%) with Non-intraepithelial lesion or malignancy according to Bethesda system.

Table 2: Cervical Pap smear findings and CD4 count in HIV positive women

CD4 count in HIV positive women	Cervical Pap smear			Total (%)
	NILM (%)	ASCUS (%)	LSIL (%)	
<400	27 (51.9)	22 (42.3)	3 (5.8)	52 (100.0)
400-600	33 (78.6)	9 (21.4)	0 (00.0)	42 (100.0)
>600	90 (96.8)	2 (2.1)	1 (1.1)	93 (100.0)
Total	150 (80.2)	33 (17.6)	4 (2.2)	187 (100.0)

Table 2 shows CD4 count and Pap smear findings. In women with CD4 count ≤ 400 / μ l there were 22 (42.3%) females with Atypical squamous intraepithelial lesion-undetermined significance, 3 (5.8%) females with Low grade squamous intraepithelial lesion and 27 (51.9%) with

Non-intraepithelial lesion or malignancy. In women with CD4 count 400/ μ l to 600/ μ l there were 9 (21.4%) females with Atypical squamous intraepithelial lesion-undetermined significance and 33 (78.6%) with Non-intraepithelial lesion or malignancy.

In women with CD4 count >600 /µl there were 2 (2.1%) females with Atypical squamous intraepithelial lesion-undetermined significance, 1(1.1%) females with Low grade squamous intraepithelial lesion and 90 (96.8%) with Non-intraepithelial lesion or malignancy.

Thus in females with CD4 count less than 400, there were 25 (48.1%) women with abnormal Pap smear while in female with CD4 count more than 400, there were 12 (8.9%) females with abnormal Pap smear. This difference was statistically significant. Chi square value=36.3, df=1, p value <0.05

The table 3 shows Sexually Transmitted disease and Pap smear findings. Atypical squamous intraepithelial lesion-undetermined and Low grade squamous intraepithelial lesion was observed

respectively in 11 (27.5%) and 2 (5.0%) females having history of sexually transmitted diseases while same was observed respectively in 22 (15.0%) and 2(1.4%) females having no history of STDs. Abnormal Pap smear was observed in 13 (32.5%) females having history of STDs while it was observed in 24(16.3%) females having no history of STD. This difference was found to be statistically significant Chi square value=5.18, df=1, p value<0.05

Table 3: Cervical Pap smear findings and history of STDs in HIV positive women

Cervical Pap smear	History of STD in HIV positive women		Total (%)
	Yes (%)	No (%)	
NILM	27 (80.0)	123 (80.3)	150 (80.2)
ASCUS	11 (15.0)	22 (18.4)	33 (17.6)
LSIL	2 (5.0)	2 (1.3)	4 (2.2)
Total	40 (100.0)	147 (100.0)	187 (100.0)

Table 4: Cervical Pap smear findings and adherence to antiretroviral therapy in HIV positive women

Cervical Pap smear	Adherence to Antiretroviral therapy				Total (%)
	80-85 %	85-90 %	90-95 %	>95 %	
NILM	14 (9.3)	10(6.7)	21 (14.0)	105 (70.0)	150 (100.0)
ASCUS	4 (12.1)	6 (18.2)	3 (9.1)	20 (66.6)	33 (100.0)
LSIL	1 (25.0)	0 (00.0)	0 (00.0)	3 (75.0)	4 (100.0)
Total	19 (10.2)	16 (8.6)	24 (12.8)	128 (68.4)	187 (100.0)

Table 4 shows detailed about Adherence to ART and Pap smear findings. **Adherence to ART** is estimated on the basis of previous month’s pills taken by the participant. It is calculated in percentage by the formula Adherence = (No. of pills consumed / no. of pills missed) X 100. The minimum value is 80% and maximum value is 100%.

Atypical squamous intraepithelial lesion-undetermined significance and Low grade squamous intraepithelial lesion was found respectively in 10 (28.8%) and 1 (2.6%) in women who had less than 90% adherence to ART while ASCUS and LSIL was observed respectively in 23 (15.1%) and 3 (1.97%) women who had more than 90% adherence to the ART.

Thus abnormal Pap smear was observed in 11 (31.4%) females who showed less than 90% adherence to ART while abnormal Pap smear was observed in 26 (17.1%) females who showed more than 90 adherence. This

difference is statistically significant. (Chi square value= 5.17, df=1, p<0.05)

DISCUSSION

Women living with HIV infection constitute one of the highest risk population subgroups for increased incidence and rapid progression of HPV-induced cervical intraepithelial neoplasia and invasive cervical cancer. [20] Various studies showed HIV-infected women have high prevalence of HPV infection, thus having greater risk of epithelial abnormality. [21]

In the present study out of 187 subjects 33 (17.7 %) had ASCUS (Atypical squamous cell undetermined significance) and 4 (2.1 %) had LSIL (Low grade squamous intraepithelial lesion). ASCUS and LSIL are at risk of development of carcinoma cervix. Thus in the present study squamous cell abnormalities were observed in 37 (19.8%) subjects. These subjects are at risk of developing cervical cancer.

With HIV/AIDS becoming a modern global pandemic, its association with cervical cancer and its precursor lesions, the present prospective study of estimating the cytological abnormalities in Pap smear in HIV-seropositive women, in our hospital gains significance. [22] In the present study the commonest epithelial abnormality was ASCUS (17.7 %), which is more than 10.52 %. reported by Gaym et al. [23]

In this study, the prevalence of LSIL was 2.1% which is less 6.3% observed by Apeksha Madan et al. [24] It is also lower than the prevalence of SIL of 10.9% in lagos [25] and 12.6 % in Enugu. [26]

In present study Cervical epithelial cell abnormalities was found to be more in participants having age above 50 years (64.71%), in widow/divorced group (21.84%), in women who married before 20 years of age (22.4%). in women belonging to Lower, Lower Middle or Middle class (22.4%). As age increases the degenerative changes occur in the epithelial cells and it may lead to cervical cancer in HIV positive women. It is also found that HIV infection is more in widow or separated women and those belonging to low socio economic status. Cervical epithelial cell abnormalities was also found more in women with parity more than two (21.1%). High incidence of squamous cell abnormalities in patients who had high parity (parity 3 or more) was also noted by B.M. Jha et al. [16] This suggests that squamous cell abnormalities are directly related to multiparity. Early sexual activities and high parity also play role in causation of cervical cancer.

In the present study in females with CD4 count less than 400, there were 25 (48.1%) women with abnormal Pap smear while in female with CD4 count more than 400, there were 12 (8.9%) females with abnormal Pap smear. This difference was statistically significant. (p value <0.05). Low level of CD4 count is associated with immunocompromised state. HIV infected women with low CD4 count may lead to HPV infection which is a precursor for

cervical cancer. HIV seropositivity and lower CD4 count are the strongest predisposing factors for the persistence of HPV. The effect of immune function studies has demonstrated that CD4 count is a significant predictor for having or developing CIN. [17,27] Study done by Chalermchokcharoenkit A et al. and Sharma A et al had shown that CD4 cell count is a significant predictor for developing CIN. [27,28]

In present study statistical association was found in abnormal Pap smear and having history of STDs in HIV infected women. STDs play role in causation cervical cancer. When STDs are present in HIV infected women, the risk for cervical cancer increases as seen in the present study

In present study, abnormal Pap smear was observed in 11 (31.4%) females who showed less than 90% adherence to ART while abnormal Pap smear was observed in 26 (17.1%) females who showed more than 90 adherence. This difference is statistically significant. (p<0.05) ART can improve the health status of HIV patients there by improves the immunological status, prevents opportunistic infections like HPV, and thereby prevents cervical epithelial abnormalities and thus prolongs the lifespan of a patients.

CONCLUSION

The prevalence of Pap smear abnormalities in HIV infected women is found to be 19.8%. Prevalence of ASCUS and NSIL was found to be 17.7 % and 2.1% respectively. Incidence of epithelial abnormalities is more with CD4 count <400. Adherence to the ART is found to associate with normal cervical epithelium. To reduce the problem of cervical cancer HIV positive women should be motivated to undergo Pap smear testing regularly. These women should adhere to the ART and should treat the STD if they have. This will help to reduce the problem of cervical cancer in women living with HIV.

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