

## SEXUALLY TRANSMITTED INFECTIONS AND CERVICAL CYTOLOGY IN HIV INFECTED WOMEN

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### ABSTRACT

#### BACKGROUND

As on 2015 Human immunodeficiency virus estimations in India, people living with HIV are 21.17 lakhs, women with HIV constituting 2/5<sup>th</sup> of the total. The prevalence of sexually transmitted infections and malignancy are more in HIV infected people. Cervical cancer is one of the leading cancers among Indian women. HIV infection and sexually transmitted infections, Human Papilloma Virus infection in particular act synergistic in predisposing to cervical neoplasia. Undetected cervical cancer may increase the mortality of HIV infected women.

#### MATERIALS AND METHODS

This is a case control study done at STI clinic of tertiary hospital of South India involving 100 HIV infected women and 50 HIV uninfected women as control. STI screening and cervical cytology was done for both the group.

#### RESULTS

Sociodemographic profile was similar for both the groups pertaining to Age, Occupation, Literacy. 80% of women in study group and control group were married and monogamous. 34% of HIV infected women had early sexual debut because of early marriage (P value .006). 86% of HIV infected and 40% of HIV uninfected women had sexually transmitted infections. (P value .000). Abnormal cervical cytology was found more in HIV infected women. Inflammatory smear was found in 65% of HIV infected women and in 42% of HIV uninfected women. Epithelial cell abnormalities were found in 25% of HIV infected women and in 2% of control group. High grade squamous intraepithelial lesion was found in 4% of study group and none in control group.

#### CONCLUSION

Prevalence of STI and abnormal cervical cytology are more common in HIV infected women. Sexually transmitted infections, HIV and HPV in particular, are the proven risk factors of cervical malignancy. So prevention of cervical cancer lies in controlling STI and preventing HPV infection by early vaccination. Screening for STI and periodic Pap smear screening should be ideally done for all HIV infected women as per NACO guidelines.

#### KEYWORDS

Cervical Cytology, Human Papilloma Virus, Sexually Transmitted Infections.

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#### BACKGROUND

As per National AIDS Control Organisation technical report 2015, the number of people living with HIV are estimated to be 21.17 lakhs. Among this, women living with HIV are estimated to constitute 8.5 lakhs constituting 2/5<sup>th</sup> of the total. Women are biologically and anatomically predisposed to contract sexually transmitted infections and HIV. HIV infected women suffers gender specific problems clinically like recurrent lower genital tract infections, cervicitis, pelvic inflammatory disease, menstrual irregularities,

malignancies of genital tract and breast. HIV infected people are more prone for malignancies. HIV, HPV and cervical pathology are related biologically and epidemiologically. Human Papilloma Virus infection has been strongly implicated as the major etiologic agent in the carcinogenesis of female genital tract. HPV induced cervical malignancy is the commonest cause of cancer related mortality among Indian women. The biological response of this agent is determined by a number of cofactors like cigarette smoking, other sexually transmitted infections like Herpes Virus infection and infections which produce a local cervicitis (Chlamydia, Gonorrhoea) and other forms of immunosuppression and the relative balance of sex steroids in the female.

It has been proved in various worldwide studies that HIV infected women have two to five times more risk of cervical intraepithelial neoplasia when compared to HIV uninfected women.<sup>1,2</sup> HIV act as a cofactor in the association between HPV infection and cervical neoplasia.

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In a meta-analysis of 15 studies it has been shown that HIV infected women have higher odds of cervical neoplasia (OR 8.8) than HIV negative women.<sup>3</sup>

Because of increased prevalence of carcinoma cervix in HIV infected women, 1993 revised classification of Centre for Disease Control and Surveillance included Invasive cervical cervix as AIDS defining condition.<sup>4</sup>

**Objectives-** The aim of the study was to compare the cervical cytology in HIV positive and HIV negative women attending STI Clinic and to determine the prevalence of abnormal Pap smears in HIV positive women and to know the prevalence of sexually transmitted infections in women with HIV infection and HIV uninfected women.

**MATERIALS AND METHODS**

This is a case control study of 100 HIV infected women and a matched control of fifty HIV uninfected women. After routine clinical examination, speculum examination was done, the nature of cervix, the nature of cervical and vaginal discharge observed and bed side tests like wet mount for trichomonas, clue cell and Candida were done. From the cervical discharge gram stain smear and culture for gonococci were done. Pap smear was done for both study group and control group using conventional PAP smear kit. The smears were wet fixed in 95% isopropyl

alcohol and sent to the pathology laboratory for staining and reporting. The smears were graded by Modified Bethesda System of Classification 2001.

- 1) Normal - No cell changes.
- 2) NILM (negative for intraepithelial changes and malignancy which includes inflammatory changes, organisms, atrophic changes and reactive changes.
- 3) ASCUS (atypical squamous cells of undetermined significance; ASC-H (atypical squamous cells cannot exclude a high-grade squamous intraepithelial lesion).
- 4) LSIL (low-grade squamous intraepithelial lesions); and
- 5) HSIL (high-grade squamous intraepithelial lesions).

**RESULTS**

95% of study group and 90% of women in control group were of sexually active age group (15- 45 years of age) ¾ of study group as well as control group were of 21-30 years of age. Nearly 50% of them were of urban domicile. 50-60% of both study group and control group were home makers. Nearly 70% of both study group and control group have low literacy level with primary school level education and below. Most of the women in control group came with genital discharge as presenting complaint (68%), whereas 40% of women in study group came for screening either with HIV positive results done outside or consequent to husband positive result.

	HIV <sup>+</sup> ve		HIV <sup>-</sup> ve		Total		Statistical Inference
	N	%	n	%	n	%	
<b>Age</b>							
15 to 20 yrs.	5	5.0%	3	6.0%	8	5.3%	X <sup>2</sup> =2.246 Df= 4.691 >0.05 Not Significant
21 to 30 yrs.	64	64.0%	28	56.0%	92	61.3%	
31 to 40 yrs.	26	26.0%	14	28.0%	40	26.7%	
41 to 50 yrs.	3	3.0%	4	8.0%	7	4.7%	
Above 50 yrs.	2	2.0%	1	2.0%	3	2.0%	
<b>Domicile</b>							
Urban	65	65.0%	29	58.0%	94	62.7%	X <sup>2</sup> =0.698 Df=1.403 >0.05 Not Significant
Rural	35	35.0%	21	42.0%	56	37.3%	
<b>Occupation</b>							
Housewives	49	49.0%	34	68.0%	83	55.3%	X <sup>2</sup> =9.154 Df=4.057 >0.05 Not Significant
Agricultural Labourer	24	24.0%	12	24.0%	36	24.0%	
House-maid	6	6.0%	1	2.0%	7	4.7%	
Sex Worker	5	5.0%	2	4.0%	7	4.7%	
Others	16	16.0%	1	2.0%	17	11.3%	
<b>Education</b>							
Illiterate	42	42.0%	17	34.0%	59	39.3%	X <sup>2</sup> =3.692 Df=5.594 >0.05 Not Significant
Can read and Write	3	3.0%	4	8.0%	7	4.7%	
Primary	25	25.0%	15	30.0%	40	26.7%	
High School	21	21.0%	10	20.0%	31	20.7%	
Higher Secondary School	4	4.0%	3	6.0%	7	4.7%	
Degree	5	5.0%	1	2.0%	6	4.0%	
<b>Marital Status</b>							
Single	2	2.0%	1	2.0%	3	2.0%	X <sup>2</sup> =11.996 Df=3.007 <0.05 Significant
Married & Living with Husband	54	54.0%	38	76.0%	92	61.3%	
Married & Separated	10	10.0%	7	14.0%	17	11.3%	
Married & Widowed	34	34.0%	4	8.0%	38	25.3%	

**Table 1. Socio-Demographic Profile**

80% of both study group and control group had monogamous sexual relationship. The interval between menarche and coitarche was significantly less in HIV infected women, in 34% of them, it was less than 2 years. 20% of HIV infected women gave past history of genital ulcer or genital discharge. On speculum examination healthy cervix was found in 52% of study group and in 68% of control group. Cervical inflammation was found in 48% of study group and among 32% of control group.

	HIV+ve		HIV-ve		Total		Statistical Inference
	n	%	n	%	N	%	
<b>Sexual History</b>							
Premarital contact	2	2.0%	1	2.0%	3	2.0%	X <sup>2</sup> =0.093 Df=2.954 >0.05 Not Significant
Extramarital contact	18	18.0%	8	16.0%	26	17.3%	
No H/o of PMC or EMC	80	80.0%	41	82.0%	121	80.7%	
<b>Profile of Initiation of Sexual Activity</b>							
Below 1yrs	15	15.0%	1	2.0%	16	10.7%	X <sup>2</sup> =12.469 Df=3.006 <0.05 Significant
1 to 2yrs	19	19.0%	5	10.0%	24	16.0%	
2 to 5yrs	44	44.0%	22	44.0%	66	44.0%	
Above 5yrs	22	22.0%	22	44.0%	44	29.3%	
<b>Previous Venereal Disease</b>							
PVD Present	20	20.0%	3	6.0%	23	15.3%	X <sup>2</sup> =5.033 Df=1.025 <0.05 Significant
PVD Absent	80	80.0%	47	94.0%	127	84.7%	

Table 2. Sexual History

Majority of women in study group (86%) had sexually transmitted infections when compared to control group (40%). The prevalence of lower genital tract infections was high (74%) among study group. In Pap smear study normal smear was found in 10% of study group, and in 56% of control group. Inflammatory smear was found in 65% of HIV infected women and 42% of HIV uninfected women. Epithelial cell abnormalities in Pap smear were found in 25% HIV infected women and in 2% of HIV uninfected women. High grade squamous intraepithelial lesion was found in 4% of study group and it was not found in control group. When the WHO clinical staging of HIV and Pap smear findings were compared, inflammatory smears and Dysplastic changes were found more among patients in clinical stage 3 and 4.

	HIV+ve		HIV-ve		Total		Statistical Inference
	n	%	n	%	n	%	
<b>Prevalence of Sexually Transmitted Infections</b>							
Candidal vulvovaginitis	18	18.0%	7	14.0%	25	16.7%	X <sup>2</sup> =47.349 Df=13.000 <0.05 Significant
Bacterial vaginosis	23	23.0%	2	4.0%	25	16.7%	
Genital Herpes	11	11.0%	1	2.0%	12	8.0%	
Trichomonas vaginalis vaginitis	9	9.0%	4	8.0%	13	8.7%	
Genital warts	3	3.0%	2	4.0%	5	3.3%	
Early latent syphilis	3	3.0%	1	2.0%	4	2.7%	
Late latent syphilis	3	3.0%	1	2.0%	4	2.7%	
Secondary syphilis	1	1.0%	0	.0%	1	.7%	
Pelvic inflammatory disease	0	.0%	2	4.0%	2	1.3%	
Molluscum Contagiosum	1	1.0%	0	.0%	1	.7%	
Non - specific genital ulcer	4	4.0%	0	.0%	4	2.7%	
No STD	14	14.0%	30	60.0%	44	29.3%	
Multiple STDs	10	10.0%	0	.0%	10	6.7%	

Table 3. Prevalence of Sexually Transmitted Infections

	HIV+ve		HIV-ve		Total		Statistical Inference
	N	%	N	%	n	%	
<b>PAP Smear Result</b>							
Normal	10	10.0%	28	56.0%	38	25.3%	X <sup>2</sup> =43.774 Df=8.000 <0.05 Significant
HPV	13	13.0%	1	2.0%	14	9.3%	
Candida	7	7.0%	2	4.0%	9	6.0%	
Trichomonas	4	4.0%	1	2.0%	5	3.3%	
Bacterial vaginosis	2	2.0%	1	2.0%	3	2.0%	
Nonspecific inflammation	39	39.0%	16	32.0%	55	36.7%	
ASCUS	5	5.0%	0	.0%	5	3.3%	
LSIL	16	16.0%	1	2.0%	17	11.3%	
HSIL	4	4.0%	0	.0%	4	2.7%	

Table 4. PAP Smear Result

## DISCUSSION

The Sociodemographic profile of both study group and control group were similar pertaining to age, social status, and literacy level. Human Papilloma Virus infection, Human immunodeficiency Virus infection have been increasingly implicated in the aetiology of genital tract malignancy. The association between sexual behaviour and cervical malignancy is well established. Early age of sexual intercourse, multiple sex partners, race, cigarette smoking, lower socioeconomic status, high parity are proven risk factors for developing cervical malignancy.<sup>5</sup>

Regarding sexual history in both the study group and control group, the history of premarital and extramarital sex was not commonly present. The difference of sexual history is not statistically significant. Most of the women in the study group were married women with monogamous sexual relationship but with a history of early initiation of sexual activity, probably because of early marriage. In our study the interval between menarche and coitarche is less in HIV infected women when compared to HIV negative women and it is statistically significant with a P value of .006. Age of sexual debut and the interval between menarche and coitarche are the most significant risk factors for development of cervical cancer. A study which estimated the relationship between risk of invasive cervical carcinoma and time since first sexual intercourse, from the International Collaboration of Epidemiological Studies of Cervical cancer, using data on monogamous women showed the Odds Ratio for cervical cancer is approximately proportional to the square of time since coitarche.<sup>6</sup> Adolescent cervix is vulnerable to get infected with HPV virus. First cervical infection with HPV often occurs soon after first sexual intercourse.

Reproductive tract infections and sexually transmitted infections commonly affect reproductive age group individuals. Ulcerative and non ulcerative STI-s increase the acquisition and transmission of HIV. Because of the epidemiological synergy between STI and HIV, naturally the prevalence of STI in HIV infected persons will be more. The increased prevalence of STI/RTI in HIV infected women has been shown in various studies. In a similar case control study, 57% of HIV infected women had STI when compared to 34% of HIV uninfected women.<sup>7</sup> In our study the prevalence of STI in HIV infected women when compared to HIV uninfected women was more and was statistically significant with a P value of .000. In our study the common STI found was Bacterial vaginosis. But in the above study candidal vulvovaginitis was common.

The increased prevalence of abnormal cervical cytology in HIV infected women has been shown repeatedly in worldwide studies. In a study by Prabha et al it is found to be 7.1%,<sup>8</sup> 34.4% by Hoicke C.<sup>9</sup> while other studies showing 26%.<sup>2</sup> and 25%.<sup>10</sup> which are comparable with our study, where we found 25% epithelial cell abnormalities in HIV infected women which is almost 10 times higher when compared to our control group of HIV uninfected women. HIV infected women have an increased rate of abnormal pap smears for both Human Papilloma Virus infections and

cervical dysplasia. In our study HPV changes were seen in 13% of study group.

## CONCLUSION

This study revealed higher rate of cervical cytologic abnormality in HIV infected women. Prevalence of sexually Transmitted infections, in particular lower genital tract infections are higher among HIV infected women. Since sexually transmitted infections (HPV) and HIV infection are important risk factors for cervical carcinoma, primary prevention of cervical carcinoma lies in controlling STI and preventing Human Papilloma Virus infection by vaccination.

On the other hand, in the antiretroviral therapy era with increased life expectancy of HIV infected people due to improved and greater accessibility to ART, the consequences of a missed or delayed diagnosis of cervical disease can be severe. Currently the only AIDS defining malignancy that can be screened and treated early is cervical carcinoma. So routine cytologic screening in HIV infected women is warranted. Pelvic examination and Pap smear examination at initial HIV evaluation followed by periodic speculum examination of cervix and pap smear every six months should be ideally done for all HIV infected women as per National AIDS Control Organisation guidelines.

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