

STUDY OF VAGINAL INFECTIONS, CERVICAL CYTOLOGY AND PREVALENCE OF MENSTRUAL PROBLEMS IN HIV INFECTED PATIENTS

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ABSTRACT: OBJECTIVE: To study vaginal infections, cervical cytology and prevalence of menstrual problems in HIV seropositive patients. **METHODS: Study Design:** hospital based non-randomized prospective observational study. **Study Type:** case control study. **SAMPLE SIZE:** 130 cases & 100 controls. **INCLUSION CRITERIA:** All married women in the age group of 20-55 yrs. Cases were taken from the seropositive women registered at the ART Centre willing to participate. Controls were HIV seronegative women attending gynaecology OPD. **RESULTS:** Out of the 130 cases, 78.4% were on ART & 21.5% were not on ART. In the present study, 87.09% of cases had abnormal Pap smear results compared to 29.09% of controls. 20% of cases had SILs compared to 8.18% of controls. Low grade intraepithelial lesions were 4.56 times more prevalent in cases. In the present study, it was found that 44.4% of SILs were found in cases with CD4 cell count <200/ μ l. When studied for lower reproductive tract infections, 54.6% of cases had LRTIs compared to 30% of controls. The most common infection was candidiasis, found in 20% cases vs. 10% controls. **CONCLUSION:** The present study has shown that the prevalence of Pap smear abnormalities & LRTIs is higher in HIV seropositive women. Hence, periodic gynaecological testing, Pap smear examination & vaginal swab testing should be done in HIV seropositive women to provide timely treatment & early identification of risk factors of malignancy.

KEYWORDS: HIV, SILs, LRTIs, Pap smear, CD4 cell count.

INTRODUCTION: Acquired immunodeficiency syndrome (AIDS) is a global pandemic with cases reported from virtually every country. Worldwide women constitute half of all people living with HIV/AIDS. For women in the reproductive years (15-44 Years), HIV is the leading cause of death and disease worldwide, yet relatively few descriptions of clinical findings associated with HIV in women have been published.

In the presence of HIV infection, particularly the immunodeficiency of AIDS, the clinical presentation, course, complications, and response to conventional therapy of sexually transmitted diseases (STDs), as well as non-infectious gynaecologic disease, may be modified resulting in excessive morbidity.⁽¹⁻³⁾

Screening for & treatment of STDs is considered an integral component of health care for patients infected with HIV, but little information is available to guide the care of female patients. The presence of an STD appears to increase the risk of both acquiring & transmitting HIV infection.^(4,5) Vaginal infections have been seen as a lesser public health priority than cervical infections. Vaginal infections, including Bacterial vaginosis (BV), T. Vaginalis, & yeast vaginitis (YV), are common among HIV-infected women.⁽⁶⁾ BV & T. Vaginalis have been shown to increase the risk of HIV acquisition among women, underscoring their importance from a public health perspective.⁽⁷⁾

Cervical cancer is the fifth most deadly cancer in women worldwide,⁽⁸⁾ despite being a preventable & curable cancer if detected early. HIV is a well-recognised co-risk factor for carcinoma

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cervix. Here comes the role of Pap smear. A large burden of HIV infection & increasing HIV epidemic in India threatens to exacerbate incidence of cervical cancer.

The background of conducting this study is due to high prevalence of HIV in Maharashtra (0.5%). The aim of this study is to compare the prevalence of RTIs, cervical cytological abnormalities & menstrual problems in HIV-infected women.

AIMS: To study vaginal infections, cervical cytology & prevalence of menstrual abnormalities in HIV seropositive women.

OBJECTIVES:

- To compare the occurrence of RTIs among HIV infected & uninfected women.
- To study & compare the cytological changes in cervical smear in HIV seropositive with HIV seronegative women.
- To study the prevalence of menstrual problems in HIV-seropositive patients.
- To correlate the results with CD4 counts & ART status.

MATERIAL & METHODS: The present study was conducted at the Department of Obstetrics & Gynaecology, GMC Nagpur from November 2011 till September 2013. It was a non-randomized, prospective, case control, observational study. Present study included a total of 240 patients, 130 cases & 110 controls.

The approval & permission of the Ethics Committee of our institute & National AIDS Control (NACO) Program was obtained. Proper consent of the study population was taken.

Inclusion Criteria:

1. All married women between the age group of 20-55yrs, attending the outpatient department of Gynaecology, & ART Centre.
2. HIV status: Cases: HIV seropositive status documented & registered at the ART clinic. Controls: HIV status tested negative at VCTC.

Exclusion Criteria:

1. Unmarried women.
2. Posthysterectomized women.

METHODOLOGY:

- Cases & controls selected after fulfilling the criteria & obtaining the consent.
- Cases were divided into 2 groups:

Group A: HIV seropositive women on ART.

Group B: HIV seropositive women not on ART.

Thorough history regarding medical, social, menstrual & treatment history as well as regarding current symptoms taken. Social history included contraceptive use, barrier usage & addictions.

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- Complete physical examination, including pelvic examination.
- Various specimens & blood samples:
 - Blood for VDRL, haemoglobin estimation, HIV testing & CD4 cell count.
 - Urine routine & microscopy.
 - Cervical swab from endocervical canal.
 - Vaginal swab from posterior fornix.
 - Pap smear.
- Viscous swabs were used to collect specimens. Pap smears were collected by cytological brush.
 - Statistical software STATA 10.0 was used for statistical analysis.

RESULTS: After thorough analysis of the data, following observations were put forward:

Among the cases, mean age was 34.9 ± 6.76 & that of the controls was 35.40 ± 9.16 . Mean parity was 1.9 ± 0.86 in cases & 1.93 ± 0.82 in controls with 65% of patients being multiparous.

Characteristics	No. of Cases (N = 130)	Percentage (%)
ART		
Yes	102	78.4
No	28	21.5
CD4 Count		
<200	18	13.8
201-500	77	59.2
>500	35	26.9
Mean CD4 count	388.81 ± 197.21 345(19-971)	
WHO Stage		
I	26	20
II	53	40.7
III	46	35.3
IV	5	3.8
Symptomatic		
Yes	59	45.3
No	71	54.6

Table 1: Characteristics of HIV-seropositive women included in the study

Out of the 130 cases, 78.4% women were on ART & 21.5% were not receiving ART. 59.2% women had CD4 cell counts between 200–500/ μl , while 13.89% had counts <200/ μl . Majority of patients belonged to WHO stage II & III, 40.7% & 35.3% respectively. 54.6% women were asymptomatic compared to 45.3% symptomatic women.

54.6% of cases were asymptomatic compared to 33.6% of controls. The most common complaint was discharge per vaginum, found in 29% of controls & 12.3% of cases. Menstrual complaints were comparable in cases & controls with respect to frequency, pattern or duration.

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When correlation between complaints & ART was studied, it was found that out of the various complaints, menstrual complaints were more common among patients on ART, 9.8% compared to 0%, indicating that immunosuppression may contribute to the menstrual abnormalities.

	Normal	Abnormal	P-VALUE	ODDS	95% C.I.
HIV-Seropositive (n=124)(%)	16(12.9)	108(87.09)	<0.001, HS	10.51	5.27- 21.47
HIV-Seronegative (n=110)(%)	67(60.9)	43(29.09)			

Table 2: Pap smear results

Out of the 130 cases, 6 had Pap smear results as unsatisfactory, hence were not included in the statistical analysis. Out of the 124 cases, 87.09% had abnormal Pap smear results compared to 29.09% of controls (P<0.001).

Pap Smear Report	CASES n=130 (%)	CONTROLS n=110 (%)	ODDS RATIO	95% C. I.	P-value
Unsatisfactory	6(4.1)	0	-	-	0.022, S
Normal	16(12.3)	67(61.8)	0.09	0.04- 0.18	<0.001, HS
Atrophic	6(4.6)	2(1.8)	2.61	0.45- 26.89	0.229, NS
Inflammatory	76(58.4)	31(28.1)	3.58	2.01-6.41	<0.001, HS
Bacterial vaginosis	33(25.3)	9(8.1)	3.81	1.67- 9.51	0.005, HS
Candida	24(18.4)	13(11.8)	1.68	0.77-3.81	0.156, NS
Trichomonas	5(3.8)	4(3.07)	1.06	0.22 -05.48	0.932, NS
Mixed	14(10.7)	5(3.8)	2.53	0.82- 9.27	0.075, NS
SILs	26(20)	9(8.18)	2.80	1.19 – 7.12	0.0097,HS
ASCUS	2(1.5)	2(1.5)	0.84	0.06- 11.82	1.000, NS
LSIL	15(11.5)	3(2.7)	4.65	1.25- 25.62	0.003, HS
HSIL	4(3.07)	3(2.7)	1.13	0.18- 7.89	1.000, NS
AGUS	4(3.07)	1(0.9)	3.46	0.33- 17.92	0.379, NS
Squamous cell Ca	1(0.7)	0	-	-	1.000, NS

Table 3: Distribution of subjects according to Bethesda classification

This table shows the detailed Pap smear results according to Bethesda system of classification, 2001. 58.4% of cases had inflammatory smear results compared to 28.1% of controls (P<0.001). Squamous intraepithelial lesions (SILs) were found in 20% of cases in comparison to 8.1% controls (P<0.0097). Low grade intraepithelial lesion (LSIL) was more common in the cases, 11.5% vs 2.7% in controls (P<0.003). In this study, no association was found between occurrence of Pap smear abnormalities & ART status.

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Pap Smear Result	CD4 COUNT		P-VALUE
	<200 n=18 (%)	>200 n=112 (%)	
Unsatisfactory	1(5.5)	5(4.4)	0.796, NS
Normal	1(5.5)	15(13.3)	0.381, NS
Atrophic	0	6(5.3)	0.328, NS
Inflammatory	8(44.4)	68(60.7)	0.194, NS
Bacterial vaginosis	3(16.6)	30(26.7)	0.421, NS
Candida	2(11.1)	22(19.6)	0.437, NS
Trichomonas	0	5(4.4)	0.374, NS
Mixed	3(16.6)	11(9.8)	0.334, NS
SILs	8(44.4)	18(16.0)	0.005, S
ASCUS	2(11.1)	0	0.018, S
LSIL	5(27.7)	10(8.9)	0.020, S
HSIL	1(5.5)	3(2.6)	0.478, NS
AGUS	0	4(3.5)	0.429, NS
Sqaumous cell Ca	0	1(0.8)	0.414, NS

Table 4: Association of Abnormal Pap smear results with CD4 count in cases

This table correlates the Pap smear results with the CD4 cell count, >200/ μ l & <200/ μ l. 18 patients had CD4 count <200/ μ l & 112 patients had count >200/ μ l. The most significant finding was the occurrence of SILs. 44.4% patients with CD4 count <200/ μ l & 16.0% patients with CD4 count >200/ μ l had SILs (P<0.005). 27.7% patients with CD4 count <200/ μ l whereas 8.9% patients with CD4 count >200/ μ l had LSIL (P<0.020). ASCUS was found in 11.1% of patients with CD4 count <200/ μ l compared to no patient with count > 200/ μ l (P<0.018).

In our study, no significant correlation was found between Pap smear abnormalities & WHO stage. Majority of patients with inflammatory results & SILs belonged to WHO stage II & III. When studied for the association of complaints with abnormal Pap smear results, it was found that 50.9% of cases had abnormal Pap smear results but no complaints compared to only 16.2% of controls.

	Present	Absent	ODDS RATIO	95% C.I.	P-VALUE
HIV-seropositive (n=130) (%)	71(54.6)	59(45.3)	2.80	1.59-4.97	0.0001, HS
HIV-seroneagative (n=110) (%)	33(30)	77(70)			

Table 5: Lower Reproductive Tract Infections

This table shows the distribution of subjects according to the presence of Lower Reproductive Tract Infections (LRTI). The LRTIs were found to be more common among the cases compared to controls, 71(54.6%) vs 33(30%) respectively (P<0.0001).

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LRTI	CASES n=130 (%)	CONTROLS n=110 (%)	ODDS RATIO	95% C. I.	P-Value
NPO*	59(45.3)	66(60)	0.55	0.32-0.95	0.024, S
BV	21(16.1)	8(7.2)	2.45	0.98=6.68	0.035, S
Candidiasis	26(20)	11(10)	2.25	1.00-5.31	0.033, S
Trichomoniasis	5(3.8)	8(7.2)	0.51	0.12-1.83	0.243, NS
Pyogenic infection	17(13.0)	5(4.5)	3.16	1.06-11.29	0.022, S
HSV	2(1.5)	1(0.9)	1.70	0.08-10.37	1.00, NS

Table 6: Lower genital tract infections in study subjects

(NPO*: No Pathogenic Organism).

Lower reproductive tract infections were found to be more common among the cases. The most common was Candidiasis found in 20% cases compared to 10% controls ($P<0.033$). 2nd most common was Bacterial vaginosis, found in 16.1% cases vs. 7.2% controls ($P<0.035$). The occurrence of LRTIs was found to be independent of ART status. Majority of cases with LRTIs belonged to WHO stage II & III.

	BV n=21(%)	YV n=26(%)	Trichomoniasis n=5(%)	Mixed n=17(%)	HSV n=2(%)
< 200	3(16.7)	2(7.6)	0	4(23.5)	2(100)
>200	18(16.0)		5(100)	13(76.4)	0
P-VALUE	0.949, NS	0.310, NS	0.31, NS	0.215, NS	0.018, S

Table 7: Association of LRTIs with CD4 count

When the occurrence of LRTI in HIV-infected women were compared with respect to CD4 count, it was found that majority of infections were found in patients with CD4 count $>200/\mu\text{l}$. In majority of studies, Candidiasis was found in HIV- infected patients with CD4 count $<200/\mu\text{l}$. But in our study, 92.3% of patients with Candidiasis had CD4 count $>200/\mu\text{l}$.

Menstrual Complaint	CASES n=10 (%)	CONTROLS n=15 (%)	ODDS RATIO	95% C. I.	P-Value
Ammenorrhoea	1(10)	0	-	-	0.400, NS
Oligomenorrhoea	2(20)	0	-	-	0.150, NS
Menorrhagia	7(70)	5(33.3)	1.19	0.31-4.92	0.072, NS
Dysmenorrhoea	0	6(40)	-	-	0.022, S
Irregular menses	0	4(26.6)	-	-	0.125, NS
Intermenstrual bleeding	0	0	-	-	-

Table 8: Distribution of subjects according to Menstrual irregularities

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Out of the 130 seropositive patients, only 10 patients had menstrual complaints compared to 15 controls. The most common complaint in the cases was menorrhagia. But there was no statistical significance.

DISCUSSION: In the present study, majority(46.2%) women were in the age group of 31-40yrs which is similar to Greenbalt et al(1999).⁽⁹⁾ When comparing the ART status, we found that 78.4% were on ART compared to 21.5% not on ART. This was similar to the findings of Prabha Devi et al(2013).⁽¹⁰⁾ In our study, 86.1% patients had CD4 cell count >200/ μ l which was comparable to the study by Vandana Goel et al(2011).⁽¹¹⁾ Majority of cases in our study belonged to WHO stage II & III, similar to the findings of Vandana Goel et al(2011).⁽¹¹⁾

In our study, 54.6% of cases had no complaints compared to 33.6 of controls. This was because of the fact that the cases were patients routinely attending the ART clinic whereas the controls were symptomatic seronegative women. The most common complaint was white discharge followed by pain in abdomen. These results were similar to the results of those of B M Jha et al (2012).⁽¹²⁾ In our study, 7.6% of cases had menstrual complaints compared to 12.7% of controls. Most common complaint was menorrhagia seen in 5.3% of cases and 4.5% of controls. Hence, no significant difference was found in the menstrual complaints or the frequency or pattern of menstrual cycle between the cases and controls. Similar findings were reported by Ellerbrock TV et al (1996)⁽¹³⁾ and Shah PN et al(1994),⁽¹⁴⁾ suggesting that neither the HIV infection nor the immunosuppression has a clinically relevant effect on menstruation.

Abnormal Pap smear results were found in 87.09% of cases vs 29.0% of controls in our study. Similar result was noted by Archana et al (2009)⁽¹⁵⁾ where 64% of cases had abnormal Pap smear results compared to 31% of controls. On further analysis of Pap smear results according to Bethesda Classification, we found that inflammatory Pap results were found in 58.4% of cases compared to 28.1% of controls, which was comparable to the results Prabha Devi et al(2013)⁽¹⁰⁾ of 74% inflammatory Pap smears in the cases.

In our study prevalence of SILs was 20% in the cases compared to 8.18% in the controls. The risk of SILs in HIV infected cases was nearly double than the controls in study by Joshi et al(2001).⁽¹⁶⁾ Of the various SILs, we found that LSIL was more common in HIV infected cases than the controls, 11.5% vs 2.7%, 3.07% cases had HSIL compared to 2.7% of controls. Similar findings were reported by B M Jha et al(2012)⁽¹²⁾ with 2.7% of cases having LSIL compared to 0% in controls, 3.19% cases vs 2% controls having ASCUS, 1.4% cases having HSIL vs 0.5% controls. In our study, no statistical significance was found between abnormal Pap smear results & ART status, similar to the findings of Prabha Devi et al(2013).⁽¹⁰⁾

The prevalence of SILs was found to be more in cases with CD4 cell count <200/ μ l than in cases with CD4 count >200/ μ l, 44.4% vs 16.0% respectively. 11.1% patients with CD4 count <200/ μ l had ASCUS, while none with CD4 cell count >200 had ASCUS. 27.7% patients with CD4 count <200/ μ l, and 8.9% patients with CD4 count >200/ μ l had LSIL. In a study by La Ruche G et al(1998),⁽¹⁷⁾ it was found that women infected with HIV-1 had increased prevalence of SILs with a decrease in CD4 cell count.

No significant correlation of WHO stages & ART status with Pap smear abnormalities was found in our study, which is in accordance to findings of the studies by Vandana et al(2011)⁽¹¹⁾ and B M Jha et al(2012).⁽¹²⁾

In the present study, the LRTIs were more common in the HIV infected cases than HIV seronegative controls, 54.6% vs 30%. This was in accordance with the findings of Archana et al

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(2009)⁽¹⁵⁾ of 57% cases having LRTIs compared to 34% of controls. 16.1% of cases had Bacterial vaginosis compared to 7.2% of controls. 20% of cases had candidiasis compared to 10% of controls. Pyogenic infection was also more common in the cases compared to controls, 13.0% vs 4.5%. Similar results were found in the study by Archana et al(2009)⁽¹⁵⁾ with 34% of cases having candidiasis compared to 14% of controls, and mixed/ pyogenic infection found in 10% of cases compared to 4% of controls.

No statistically significant association was found of LRTIs with CD4 count, ART status & WHO stage in cases. This is in accordance with the findings of the study by Vandana et al (2011).⁽¹¹⁾

CONCLUSION: From our study, we conclude that optimal screening strategies should be implemented for the frequent and regular gynaecological examination of HIV infected women. The prevalence of Pap smear abnormalities & LRTIs was found to be higher in HIV infected women. Significant findings were reported in women who were asymptomatic at the time of examination, underscoring the need of routine testing for LRTIs & early identification of risk factors for malignancy in this group.

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