



CERVICAL CANCER SCREENING IN HIV POSITIVE FEMALES USING LIQUID BASED CYTOLOGY IN A TERTIARY CARE CENTRE OF CENTRAL INDIA.

Pathology

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ABSTRACT

Context: Cervical cancer & Human Immunodeficiency Virus (HIV) infection both are important public health Centers for Disease Control and Prevention (CDC) in 1993. HIV-infected females are more likely to show abnormal Pap smear results such as squamous cell carcinoma (SCC), high grade squamous intraepithelial lesion (HSIL) and low grade squamous intraepithelial lesions (LSIL). Because of early detection with Papanicolaou (Pap) smear screening and colposcopy, efficient medication, and preventive methods such as vaccine, the incidence of cervical cancer-related death and morbidity has decreased dramatically over the years. **Aims:** To evaluate prevalence of cervical dysplasia and cervical carcinoma in HIV positive females. **Setting and Design:** Prospective observational study **Method and Material:** Cervical samples collected from total 250 females attending ART centre of Gandhi medical college and Hamidia hospital Bhopal. A low cost LBC “Ezprep” used for processing LBC samples. **Result:** In present study, prevalence of epithelial abnormalities was found to be 11.6% amongst HIV positive females. The epithelial abnormalities were found to be more prevalent in the age group of 30-39 years in present study suggesting that the risk of cervical cancer is present in HIV positive females even in younger age group. Multiparity and decreased CD4 count status in HIV positive females have also been found to be significantly associated with epithelial abnormalities. **Conclusion:** The high prevalence of epithelial abnormalities in HIV-positive women in present study supports the recommendation of Center for Disease Control and WHO for regular gynaecological examination, including Pap smear in all of these women, even if they have no gynaecological symptoms.

KEYWORDS

HIV, Cervical cancer screening, Liquid Based Cytology.

INTRODUCTION

Cervical cancer & Human Immunodeficiency Virus (HIV) infection both are important public health problems in developing countries^[1]. The Human Papilloma Virus (HPV) is the most well-known etiologic agent causing cervical cancer. HIV-positive women have a greater risk of cervical intraepithelial neoplasia caused by the human papillomavirus (HPV).^[1]

Vulvo vaginal candidiasis, Cervical dysplasia, Cervical cancer and Pelvic inflammatory disease (PID) were added to the revised arrangement of HIV infection under category B^[2].

Cervical cancer is also more common and more aggressive in HIV-positive women. Cervical Cancer was added to the list of AIDS-defining malignancies by the Centers for Disease Control and Prevention (CDC) in 1993.^[3]

HIV-infected females are more likely to show abnormal Pap smear results such as squamous cell carcinoma (SCC), high grade squamous intraepithelial lesion (HSIL) and low grade squamous intraepithelial lesions (LSIL).^[4]

As a result, the CDC recommends that all HIV-positive women get a full gynaecological checkup, including a pap smear, when they are first diagnosed or seek pregnancy care.^[5] Carcinoma Cervix, unlike most other cancers, is highly preventable when precursor lesions are identified and treated before they progress to malignancy.

Liquid-based cytology (LBC) involves rinsing the sampling device in a vial of liquid to make a cell suspension, which is then used to create a cell layer on a slide. Mucus, blood, and debris that obstruct the view of cells on a conventional pap smear are removed. Slides created in this manner can be read faster than conventional pap smear slides. The main advantages of this LBC technique are that it reduces the number of insufficient smears and provides enough cells for molecular biology techniques to detect infectious agents such as human papillomavirus (HPV), Chlamydia trachomatis, N. gonorrhoea, and others.

MATERIAL AND METHOD:

Sample Size: 250 HIV positive females

Sample Collection: Cervical samples collected from HIV positive females attending ART centre of Gandhi medical college and Hamidia hospital, Bhopal after taking informed consent.

Ethical Consideration: The study was approved by institutional's ethics committee.

Sample Collection Method:

Informed consent was taken from the patient and patients were counselled about the details and benefits of cervical screening procedure.

Strict confidentiality of the patients were maintained throughout the study.

- Detailed history of the patient was taken
- General examination and pelvic examination were performed. Per speculum examination was performed to assess cervix.
- The patient was placed in lithotomy position. Cervical samples were collected using endocervical brush.
- Cervix Brush head was broken in the Ezi prep LBC vial, which contained 20 ml of alcohol-based fixative solution.

Processing Of Liquid Based Cytology Sample:

- A low cost LBC “Ezi prep” manual kits were used for processing of LBC samples.
- After getting the smear this monolayer smear was directly stained using pap stain.
- Smears were reported using Bethesda system of cervical cytology 2014.

OBSERVATIONS AND RESULT:

Following are the observations we came across in present study:

Table 1: Results of liquid based cytology according to Bethesda system of cervical cytology 2014

LIQUID BASED CYTOLOGY	Frequency	Percent
INADEQUATE	1	0.4
NILM	89	35.6
NILM INFLAMMATORY	59	23.6
NILM BACTERIAL VAGINOSIS	50	20.0

NILM TRICHOMONAS	5	2.0
NILM BACTERIAL VAGINOSIS TRICHOMONAS	6	2.4
NILM CANDIDA	6	2.4
NILM ACTINOMYCES	1	0.4
NILM ATROPHIC	4	1.6
ASCUS	2	0.8
ASC-H	1	0.4
LSIL	7	2.8
HSIL	14	5.6
SCC	5	2.0
Total	250	100.0

0.4% smears were unsatisfactory for evaluation. 35.6% cases had no inflammation and no epithelial abnormalities. 23.6% cases were categorized under NILM inflammatory category. Under NILM organism category, 20% cases had Bacterial vaginosis, 2% had trichomonas infection and 2.4% cases had mixed infection of bacterial vaginosis and trichomonas. 2.4% cases had candida and 1 case had bacteria morphologically consistent with actinomyces. 29 cases were diagnosed to have epithelial abnormalities. Amongst epithelial abnormalities, 0.8% cases were categorized under ASCUS category, 0.4% as ASC-H, 2.8% as LSIL, 5.6% as HSIL and 2% as Squamous cell carcinoma.

Table 2: Age wise distribution of various lesion identified in Liquid based cytology

Age Group	Epithelial abnormalities (Liquid Based Cytology)			Total
		Present	Absent	
20-29 Years	Count	1	41	42
	%	3.4%	18.6%	16.8%
30-39 Years	Count	11	100	111
	%	37.9%	45.2%	44.4%
40-49 Years	Count	9	57	66
	%	31.0%	25.8%	26.4%
50-59 Years	Count	6	16	22
	%	20.7%	7.2%	8.8%
≥60 Years	Count	2	7	9
	%	6.9%	3.2%	3.6%
	Count	29	221	250
	%	100.0%	100.0%	100.0%
Pearson Chi-Square	Value	df	P Value	Result
	10.317a	4	0.035	Significant

In the present study, majority of the females were between age group 30-39 years. Second most common age group was 40-49 years. Only 9 females were above 60 years of age. Out of all the epithelial abnormalities diagnosed, 37.9% cases were diagnosed in the age range of 30-39 years, 31% cases were diagnosed in the age range of 30-39 years. 1 female of 28 years age was diagnosed as LSIL. P value was less than 0.05 and significant association was seen between age and epithelial abnormalities suggesting that the prevalence of epithelial abnormalities in more in less than 49 years of age in HIV positive females. (Table 2)

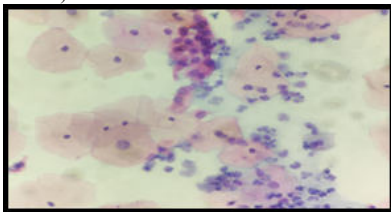


Image 1: shows HSIL: cells are having high N:C ration showing mild pleomorphism and nuclear irregularity (LBC).

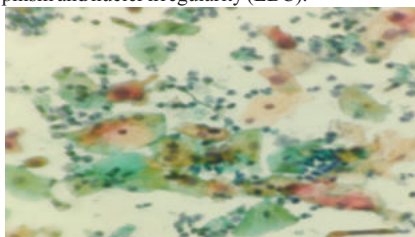


Image 2: Squamous cell carcinoma; Pleomorphic tumour cells along with tadpole cells in the background of tumour diathesis

DISCUSSION:

With the increasing prevalence of HIV/AIDS and its link to cervical cancer and its precursor lesions, the current prospective study of cervical cancer screening in HIV-positive women by Liquid based cytology in our hospital gains significance.

A total of 250 HIV positive females attending ART centre of our hospital were screened for cervical cancer using Liquid based cytology.

Epithelial abnormalities in HIV positive females:

Table 3: Studies comparing prevalence of various epithelial abnormalities in HIV positive females

Study	No epithelial abnormality	Epithelial abnormality	ASCUS	ASC-H	LSIL	HSIL	SCC	AGUS+
Chalermchockcharoenkit et al.[6] (n=821)	84.6%	15.4%	2.8%	0.6%	8.5%	3.5%	0	0
Bagga et al.[7] (n= 136)	89.7%	10.3%	1.5%	0%	5.9%	2.2%	0.7%	0
Gaym et al.[8] (n=466)	83.4%	16.9%	10.52%	0%	5.15%	4.36%	0	0
Liebenson et al. [9] (n = 84)	79.76%	20.24%	0%	0%	19.05%	1.19%	0	0
Devi et al. [10] (n=252)	92.86%	7.14%	0.8%	0%	4.37%	1.2%	0	0.8%
Jha et al.[1] (n= 407)	87.8%	8.34%	3.19%	0.73%	2.7%	1.47%	0	0.25%
Vani et al.[11] (n=100)	80%	20%	5%	0%	11%	2%	1%	1%
Madan et al.[4] (n=238)	87.39%	12.6%	4.62%	1.68%	2.10%	3.36%	0.8%	0%
Kavitha et al.[12] (n=100)	95%	5%	0	0	3%	0	2%	0
Present study (LBC)	88.4%	11.6%	0.8%	0.4%	2.8%	5.6%	2%	0

In present study, 11.6% females had epithelial abnormalities which included ASCUS 0.8%, ASC-H 0.4%, LSIL 2.8%, HSIL 5.6% and squamous cell carcinoma 2%. Various studies comparing prevalence of various epithelial abnormalities in HIV positive females are depicted in table 3.

A study by Chalermchockcharoenkit et al. (2011) who screened 821 HIV positive females and found that the prevalence of cervical squamous cell abnormalities was 15.4%, out of them ASCUS was 2.8%, atypical squamous cells cannot exclude high grade squamous intraepithelial lesion (ASC-H) 0.6%, LSIL 8.5%, and HSIL 3.5%.^[6]

Devi et al (2013) found a prevalence of abnormal Pap smears of 7.17 percent in HIV positive females, which is a twofold greater risk when compared to the general population.^[10]

Maiman et al (1998) found that in HIV positive females, 30–60% of Pap smears show cytological abnormalities and 15–40% have indications of dysplasia.^[13]

The disparities between this study and others could be related to the diverse social backgrounds and sample sizes, as well as the varying stages of HIV infection and age groups sampled.

Table 4: Studies comparing the prevalence of various organism in HIV positive females

Specific infections	Sample size	Bacterial vaginosis	Trichomonas	Mixed infection(Bacterial vaginosis + Trichomonas)	Candida	Bacteria morphologically consistent with actinomycetes
Chopra et al.[14]	150	2%	8%	4%	2%	0
Chalermchokcharoenkit et al.[6]	821	0.2%	1.6%	0%	19.4%	0
Kavitha et al.[12]	100	8%	1%	0%	7%	0
Gupta et al.[15]	150	3.03%	0%	0%	2.27%	0
Madan et al.[04]	250	2.1%	1.68%	0%	2.52%	0
Sharma et al.[16]	83	0%	12%	0%	34%	0
Goel et al.[17]	40	50%	0%	0%	18%	0
Jha et al. [1]	407	29.39%	0.5%	2.01%	1.78%	0
Present study (LBC)	250	20%	2%	2.4%	2.4%	0.4%

In HIV, the coexistence of reproductive tract infections (RTIs) is mostly acquired through heterosexual interaction. (Madan et al.)^[4]

In present study, 20 % females had bacterial vaginosis, 2% females had trichomonas, 2.4% females had mixed infection of bacterial vaginosis + trichomonas, 2.4% females had candida and 0.4% females had actinomycetes.

Similar findings were seen in the study by Jha et al. in which 29.9% females had bacterial vaginosis, 0.5% females had trichomonas, 2.01% females had mixed infection and 1.78% females had candida.^[1] (Table 4)

All these findings suggest that, in HIV-positive women, the prevalence of reproductive tract infection is high enough to urge routine gynecologic examination and reproductive tract infection screening

CONCLUSION:

- With the increasing prevalence of cervical cancer and HIV/AIDS, the present study aims at screening cervical cancer amongst HIV positive females by Liquid based cytology.
- In present study, prevalence of epithelial abnormalities was found to be 11.6% by liquid based cytology.
- The epithelial abnormalities were found to be more prevalent in the age group of 30-39 years in present study suggesting that the risk of cervical cancer is present in HIV positive females even in younger age group. Multiparity has also been found to be significantly associated with epithelial abnormalities.
- The high prevalence of epithelial abnormalities in HIV-positive women in present study supports the recommendation of Center for Disease Control and WHO for regular gynaecological examination, including Pap smear in all of these women, even if they have no gynaecological symptoms.
- As a result, low cost LBC has potential as a more effective screening approach in low-resource settings, such as developing countries like India, where women are at high risk for cervical cancer.
- WHO has introduced HPV testing as primary method of cervical cancer screening amongst HIV positive females. LBC offers additional ancillary testings such as HPV DNA testing and immune markers in the same sample. So separate sample collection for HPV testing is not required.
- To conclude, Prevalence of cervical epithelial abnormalities is high in HIV positive females, therefore all the HIV positive females should be regularly screened for cervical cancer.

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