Cervical Screening in HIV Positive Females: A Cross Sectional Study

Pratibha Chadar[1], Priya Singh Suryvanshi[2], Juhi Agrawal[3], Sushruta Shrivastava[4], Himani Rai[5]

[1,2]Senior Resident, Department of Obstetrics and Gynaecology, Kamla Raja Hospital, Gajra Raja Medical College, Gwalior, Madhya Pradesh, India

[3]Professor, Department of Obstetrics and Gynaecology, Gandhi Medical College, Bhopal, Madhya Pradesh, India

[4]Assistant Professor, Department of Obstetrics and Gynaecology, Gandhi Medical College, Bhopal, Madhya Pradesh, India

[5]Senior Resident, Department of Pathology, Gandhi Medical College, Bhopal, Madhya Pradesh, India

Abstract:

Background: Cervical cancer is a leading cause of AIDS-defining illness, and HIV-positive women worldwide. Detection of cervical cancer in precancerous stage is 100% curable.

Aim: To determine the rate of cervical screening among HIV-positive women and compare the performance of screening tests and assesses factors affecting participation

Methods: HIV-positive women aged 30–59 years attend the anti-retroviral therapy (ART) clinics were screened by conventional Pap, HPV testing (Hybrid Capture 2) and visual inspection with acetic acid (VIA). A cohort of HIV-negative women from the community matched for age and parity were screened similarly. Screen-positive women underwent colposcopy and biopsy. Factors affecting participation were assessed

Results: Out of total cases majority of them (44.4%) belonged to 30-39 years age group. Most of the participants (96.8%) were unaware about cervical screening, 97.2% were housewives and 74.4% belonged to upper lower socio-economic status. The mean parity of was 2.15±1.29 and maximum (69.2%) females were multiparous. Conventional smear and LBC revealed concordant findings in 16.7%, 100%, 85.7% and 100% cases of ASCUS, LSIL, HSIL and SCC respectively (p<0.05). Among the screening methods, sensitivity and negative predictive value was 100% for detection of abnormal cytology for liquid-based cytology whereas VILI had highest specificity. Overall, diagnostic accuracy washighest for liquid-based cytology.

Conclusion: Risk of cervical cancer was higher in HIV infected women. Frequent screening of these patients for cervical cancer can reduces the morbidity and mortality among women.

Keywords: HIV Infection, Cervical Screening, Cervical Cancer, Conventional Pap Smear.

Introduction

Human immunodeficiency virus (HIV) infection is caused by retrovirus which attacks the immune system of the patient and in end stage it leads to Acquired Immunodeficiency Syndrome (AIDS) [1]. HIV infection transmits through sexual intercourse, body fluids i.e., via blood or mucosal secretions, sharing infected needles and vertically from mother to infant [2].

According to The Joint United Nations Programme on HIV/AIDS (UNAIDS) there are approximately 37.7 million people living with HIV, of which 53% are women [3]. In India, approximately 23.49 lakh are reported to be suffering from HIV of them approximately 39% are women [4]. The HIV virus is a lymphotropic virus which infects and destroys CD4+ T cells and replicates inside the lymph nodes

eventually weakening the immunity system of the patient [5]. Globally, cervical cancer is the second most common cancer among females [6]. Multiple sexual partners, early age of first sexual activity, the use of hormonal contraceptives, smoking, HPV, and HIV infections are significant risk factors for cervical cancer [7]. For the early detection of cervical cancer, various screening methods such as PAP smear, Colposcopic examination, liquid based cytology, visual inspection of cervix after applying acetic acid (VIA) or Lugol's Iodine (VILI), HPV testing, automated cervical screening technique etc. have been recommended [8].

As a result of the association between HIV and CIN, the Royal College of Obstetricians and Gynaecologists recommends more frequent

cervical screening for women with HIV infection in the form of annual cytology [9]. Cervical screening programmes are dependent on good participation of the target population. Given the increased risk of CIN in women with HIV infection, a high uptake of cervical screening is particularly important in this high risk group.

VIA has been recommended to be included as a primary screening tool for cervical cancer screening by Government of India. Screening for cervical cancer in HIV-positive women is extremely important due to the high burden of HIV disease in women [10, 11].

Hence, prevention, early detection, and treatment of cervical neoplasia are integral components of the management of HIV-infected women [12]. Cervical cancer is a leading cause of death among women worldwide. Cervical screening has reduced the incidence of cancer cervix in many advance countries [13]. It has got a long pre-invasive state which could be detected and treated. So, screening is highly effective.

Aims and Objectives

This study evaluates the prevalence of cervical cancer; determine sensitivity & specificity of Liquid Based Cytology and Visual Inspection with Acidic Acid for cervical cancer screening in HIV infected women.

Materials and Methods

This cross sectional observational study was carried out in the Department of Obstetrics and Gynaecology, Sultania Zanana Hospital, Gandhi Medical College, Bhopal (M.P.). Study duration was one years (1st August 2020 to 31st July 2021)

Inclusion criteria:

- All known HIV positive females attending ART Centre
- Women ≥20 years of age
- Patients who provide written consent for the study

Exclusion criteria:

- HIV negative females
- Women <20 years of age
- Patients who not provide consent for the study

Detailed data regarding Sociodemographic variables such as age, marital status, occupation and socioeconomic status and detailed history regarding duration of HIV, mode of transmission, presenting complaints, menstrual cycle, marital and obstetrics history and other significant history was obtained from all the study women.

All patients were subjected to general examination (vital & anthropometric parameters), systemic examination was conducted and findings were recorded.

Local examination was conducted using Per Speculum Examination and appearance of cervix, discharge and erosions etc. were recorded.

Liquid based cytology sample was obtained initially and then VIA and VILI was done. Bethesda system was used for cervical cytological analysis.

Table 1: Bethesda system for scoring cervical cytology [14]

Histology		Cytology
Dysplasia	CIN	Bethesda
Normal	Normal	Within normal limits
Benign atypia	Inflammatory atypia	Benign cellular changes
Atypical cells	Squamous atypia	ASCUS
Mild dysplasia	CIN I	Low grade SIL
Moderate dysplasia	CIN II	High grade SIL
Severe dysplasia	CIN III	High grade SIL
Carcinoma in situ	CIN III	High grade SIL
Microinvasive (cancer)	Microinvasive (cancer)	Microinvasive (cancer)

Statistical analysis: Statistical analysis was performed using IBM statistical package for the social sciences (SPSS) statistics (version 20.0). Descriptive analysis was done to show the distribution in the form of frequency and percentage P-value <0.05 was considered as statistically significant.

Results

A total of 250 HIV positive females meeting inclusion criteria were enrolled in this study, out of that majority of them (44.4%) belonged to age group of 30 to 39 years, with mean age were 38.01±9.18 years. Most of the participants (96.8%) were unaware about cervical screening.

Majority of the patients (97.2%) were housewives and 74.4% belonged to upper lower socio economic status. The mean age of attaining menarche was 13.43±0.93 years, the mean parity of was 2.15±1.29 and maximum (69.2%) females were multiparous.

Table 1: Distribution of patients according to Sociodemographic variables

Sociodemographic Variables		Frequency (n=250)	Percentage
Age (years)	20 - 29	42	16.8%
	30 -39	111	44.4%
	40 -49	66	26.4%
	50 - 59	22	8.8%
	≥ 60	9	3.6%
	Mean±SD	38.01±9.18	
Awareness of cervical screening	No	242	96.8%
	Yes	8	3.2%
Occupation	Housewife	243	97.2%
	Laborer	4	1.6%
	Maid	3	1.2%
Socio-economic status	Lower middle	7	2.8%
	Upper lower	186	74.4%
	Lower	57	22.8%
Menarche age	11 – 13	131	52.4%
	14 – 16	119	47.6%
	Mean	13.43±0.93	
Parity	0	15	6%
	1	62	24.8%
	2	97	38.8%
	3	42	16.8%
	≥4	34	13.6%
	Mean	2.15±1.29	
Contraceptives	No	248	99.2%
	OCP	1	0.4%
	Tubectomy	1	0.4%
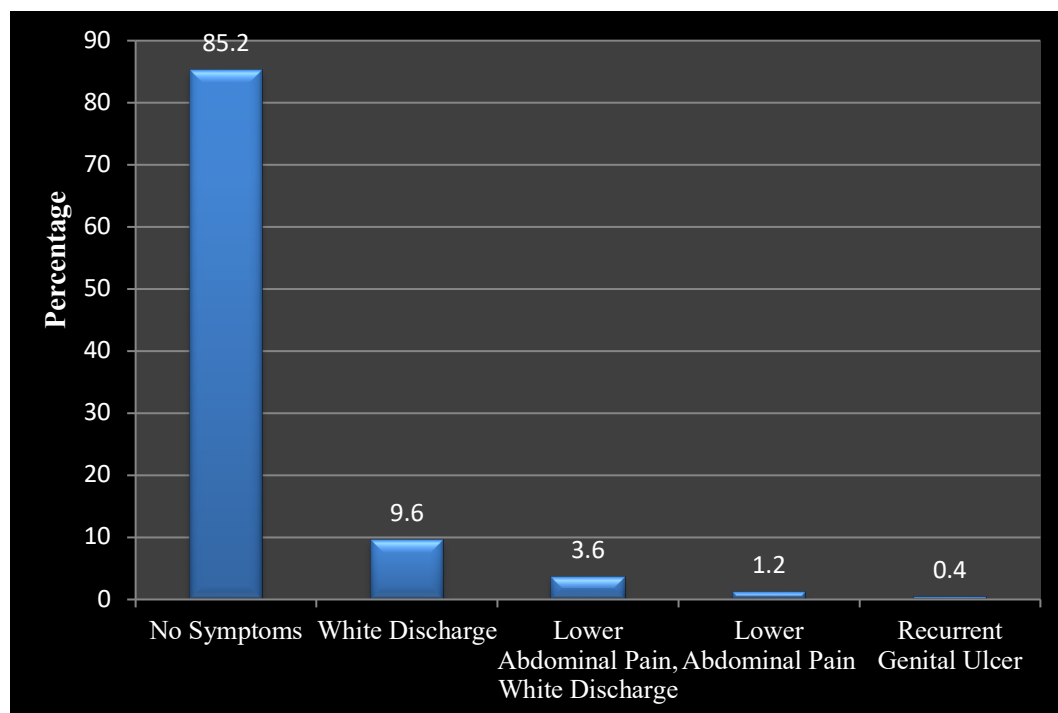
Figure 1: Distribution of patients according to symptoms

In present study, history of blood transfusion was documented in 3.2% cases whereas husband was HIV positive in 86.4% cases. History of multiple sexual partners was negative in 70% cases whereas 30% cases were not willing to disclose the infor- mation. Husbands of majority of the patients were laborers (64.4%) and 20.4% were drivers. Private job was done by 7.6% husbandswhereas 4.8% were farmers and 1.2% each were shopkeepers and tai- lors. There is no history of HIV in the family for

98% of the patients and only 2% had history of   HIV in their family.

Table 2: Distribution of patients based on risk factors

Risk factor		Frequency (n=250)	Percentage
History of blood transfusion	No	242	96.8%
	Yes	8	3.2%
History of multiplesex partner	No	175	70%
	No history given by patient	75	30%
Husband HIV status	Negative	34	13.6%
	Positive	216	86.4%
Occupation of husband	Driver	51	20.4%
	Farmer	12	4.8%
	Laborer	161	64.4%
	Private job	19	7.6%
	Shopkeeper	3	1.2%
	Tailor	3	1.2%
	Teacher	1	0.4%
History of HIV in family	No	245	98%
	Yes (Child)	5	2%

Out of 7 cases with inadequate smear on conventional smear, liquid based cytology also observed inadequate results in 14.3% cases. Conventional smear and LBC revealed concordant findings in 16.7%, 100%, 85.7% and 100% cases of ASCUS, LSIL, HSIL and SCC respectively (p<0.05)

Table 3: Association between conventional smear and liquid basedcytology

LBC	Conventional smear					
	Inadequate (n=7)	Inflammatory (n=218)	ASCUS (n=6)	LSIL (n=2)	HSIL (n=14)	SCC (n=3)
Inadequate	1 (14.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Inflammatory	5 (71.4)	215 (98.6)	0 (0)	0 (0)	0 (0)	0 (0)
ASCUS	0 (0)	1 (0.5)	1 (16.7)	0 (0)	0 (0)	0 (0)
LSIL	0 (0)	2 (0.9)	3 (50)	2 (100)	0 (0)	0 (0)
HSIL	1 (14.3)	0 (0)	2 (33.3)	0 (0)	12 (85.7)	0 (0)
SCC	0 (0)	0 (0)	0 (0)	0 (0)	2 (14.3)	3 (100)

P=0.001

Out of 25 cases with abnormal conventional smear, VIA was positive in 52% cases, VILI was positive in 28% and LBC also revealed abnormal cytology in 100% cases. Thus this method can be use as reliable cervical screening method where LBC is not available.

Table 4: Association of findings of Conventional smear with variousmethods

		Conventional smear		P value
		Normal (n=215)	Abnormal (n=25)	
VIA	Negative	222 (98.7%)	12 (48%)	0.001
	Positive	3 (1.3%)	13 (52%)	
VILI	Negative	223 (99.1%)	18 (72%)	0.001
	Positive	2 (0.9%)	7 (28%)	
LBC	Normal	221 (98.2%)	0 (0%)	0.001
	Abnormal	4 (1.8%)	25 (100%)	

Our study revealed that out of 3 screening methods, sensitivity and negative predictive value was 100% for detection of abnormal cytology for liquid based cytology whereas VILI had highest specificity. Overall, diagnostic accuracy washighest for liquid based cytology.

Table 5: Diagnostic accuracy of VIA, VILI and LBC

	VIA	VILI	LBC
Sensitivity	52	28	100
Specificity	98.7	99.1	98.2
PPV	81.25	77.8	85.2
NPV	94.9	92.5	100
Diagnostic accuracy	94	92	98.4

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.

Presents study found Majority of the females belonged to age group of 30 to 39 years, with mean age of 38.01±9.18 years, concordant to findings of Boddu A et al [15] and Kelly HA et al [16].

In our study majority of the patients belonged to lower socioeconomic status and most of the women was housewife, similar results shown by Naidu NP et al [17].

A study done by Denning, et al [18] observed inverse relationship of HIV with socioeconomic status, i.e. the prevalence of HIV increased in patients with lower socioeconomic status.

Sexual behaviour and multiparty have been suggested as the risk factor for cervical cancer in females with HIV in this study, in agreement with the Shamsundar S, et al [19].

We have noted that the majority of females were asymptomatic and abdominal pain, white discharge and history of recurrent genital ulcer were the common clinical symptoms, consistent findings seen by S Shah, et al [20] and Nakamura A, et al [21].

This is the point of concern as females must be made aware regarding the HPV infection and risk of other opportunistic infection. Very less number of participants were aware regarding the HIV infection and cervical screening, whereas Mokhele I et al [22] in their study reported much higher awareness in females with HIV for cervical screening but the awareness regarding HPV infection was much lower.

The common risk factors for HIV infection were history of blood transfusion, multiple sex partner, occupation of husband, and history of HIV in family, accordance with the Korn AK, et al [23].

Present study reported that Conventional smear and LBC revealed concordant findings in 16.7%, 100%, 85.7% and 100% cases of ASCUS, LSIL, HSIL and SCC respectively (p<0.05), our results was comparable with the other researchers like: Chakravarty J et al [24] and Rahatgaonkar VG, et al [25].

We assessed the role of VIA, VILI and LBC against conventional smear for screening of cervical epithelial lesions in patients with HIV. Liquid based cytology was concordant to conventional smear for diagnosis of ASCUS, LSIL, HSIL and SCC in 16.7%, 100%, 85.7% and 100% cases respectively, these observation correlate with the S Maria, et al [26].

Bhattacharya AK et al [27], documented the sensitivity of 89%, specificity of 78.7% for VIA for detection of cervical lesions.

Singh U et al [28], reported LBC to be superior to conventional cytological method for detection of SCC recurrence.

We observed that advancing age particularly in the reproductive age (30 to 49 years), late age at menopause, higher parity and low CD4 count (<500) as significant predictor of abnormal cytology in patients with HIV suggesting immunodeficiency and hormonal status predicting the risk of cervical cancer in HIV patients, accordance with the Stainley MA et al [29].

Conclusion

We have concluded that age range of 30 to 49 years, late age at menopause, higher parity and low CD4 count are significant predictor of abnormal cytology in patients with HIV.

Increasing the frequency of cervical screening of HIV infected females can helped in earlier detection of cancer cervix more effectively reduce the morbidity and mortality associated with HPV infection in HIV positive females

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