Original Research Article

A study of prevalence of Pap smear abnormalities in HIV seropositive women

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Abstract

Background: Cervical Cancer is the fourth most common cancer in women worldwide. Studies now clearly demonstrate an increased risk of precancerous cervical lesions and a more rapid progression to cancer amongst HIV infected women particularly those with low CD4 cell counts or decreasing immunity.

Objective: To determine the prevalence of abnormal Pap smears in HIV-positive women and to correlation between CD4+ cell count and abnormal Pap smear among HIV infected women.

Materials and methods: This was a cross-sectional descriptive study included all HIV positive women,18-69 years who had been or were sexually active and were attending the HIV clinic and consented to participate in the study and have a pap smear done to them.

Results: From 20-08-2015 to 20-10-2016 a total of 100 women infected with HIV had cervical smear taken for cytology. Of the 100 who were recruited for the study, cervical SIL were present in 20 (20%) of those with cervical SIL, 11 (11%) women had low-grade SIL, 5 (5%) had ASCUS, 2 (2%) had high-grade SIL, 1 (1%) had SCC and 1 (1%) had AGC-H. A CD4 lymphocyte count of <200 cells/mm^3 was found to be significantly associated with cervical SIL.,WHO stage 4 was found to be statistically significant association with cervical SIL, use of HAART was found to be associated with cervical SIL.

Conclusion: A high prevalence of cervical SIL was found among HIV-infected women. Increased immune suppression was significantly associated with cervical SIL.

Key words

Pap smear, HIV seropositive, Women, Prevalence.

Introduction

Cervical Cancer is the fourth most common cancer in women worldwide. Studies now clearly demonstrate an increased risk of precancerous cervical lesions and a more rapid progression to cancer amongst HIV infected women particularly those with low CD4 cell counts or decreasing immunity. Effective cytological screening and follow up intervention programs have been credited for the sharp decline in its prevalence in Europe and North America. This has not been the case in the developing world where resources and infrastructure have proved insufficient to offer quality screening and appropriate follow-up.

Cervical Cancer is the 4th most common cancer in women & the seventh overall, with the estimated 5,28,000 new cases (both sexes combined) in 2012. Although the annual number of cases has increased carcinoma of the cervix has declined in relative importance. It was the second most common cancer of women in 1975. As with Liver cancer, a large majority (around 85%) of the global burden occurs in the less developed regions, where it accounts for almost 12% of all female cancers. High risk regions, with estimated ASRS over 30 per 1,00,000 include Eastern Africa (42.7), Melanevia (33.3), Southern (31.5), and Middle Africa (30.6). Rates are lowest in Australia/ Newzealand (5.5), and western Asia (4.4). Cervical cancer remains the most common cancer in women in Eastern and Middle Africa. There were an estimated 2,66,000 deaths from cervical cancer worldwide in 2012, accounting for 7.5% of all female cancer deaths. Almost nine in 10 (87%) cervical cancer deaths occurs in less developed regions. The average risk of dying from cervical cancer before age 75 is three times higher in the less than in more developed regions. Mortality varies 18 Fold between the different regions of the world ranging from less than 2 per 1,00,000 in western asia, western Europe, and Australia/ New Zealand to above 20 per 1,00,000 in melanesia (20.6) Middle (22.2) and Eastern 27.6 and Africa [1]. Human papillomavirus (HPV) is known to play an important etiological role in the development of cervical cancer. To date more than 100 HPV types have been characterized based on nucleotide sequence and approximately 40 distinct HPV types are known to infect the genital tract. Based on the strength of their association with cervical cancer, mucosal types of HPV are classified as low – risk or high – risk [2]. HPV genotypes that have only rarely or not been found in invasive cervical cancers are defined as low risk types they include HPV 6 and HPV 11. High risk types such as HPV (16, 18, 45, 31, 33, 45, 52, 58, 35 and 51] are among most types found in invasive cervical cancers and are the main factors implicated in cervical carcinogenesis [3]. Worldwide, the human papillomavirus (HPV) has been detected in more than 90% of cervical carcinomas and in as many as 99.7% of cervical neoplasias [4]. Because HPV is implicated in such a high percentage of cervical cancers, a great deal of research has been devoted to characterizing the virus and its role in cervical cancer. HPV is now known to be a small deoxyribonucleic acid (DNA) virus that infects epithelial cells and causes a variety of skin lesions. To date, more than 100 different types of HPV have been identified, 40 of which may involve lesions of the anogenital tract. Subtypes of the virus can be broadly divided into those that infect stratified squamous epithelium and those that infect mucosal epithelium. The mucosotrophic types can be further subdivided into low-risk and high-risk types. Of those that affect genital tissues, the low-risk types have been associated with the formation of genital warts. The commonly identified low-risk types include 6, 11, 40, 42, 43, 44, 54, 61, 72, and 81. The high-risk types are those associated with the formation of intraepithelial neoplasia and include 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 69, and 82.

Materials and methods

This was a cross sectional descriptive study whose aim was to determine the prevalence of cervical cytology abnormalities in HIV infected women at Govt. Maternity Hospital,

Hanamkonda from 20-08 -2014 to 20-10-2016.

Inclusion criteria

All HIV positive women,18-69 years who had been or were sexually active and were attending the HIV clinic and consented to participate in the study and have a pap smear done to them.

Exclusion criteria

History of hysterectomy, Clients who were not willing to participate in the study, Women with obvious cancer of the cervix and pregnant and postnatal mothers were excluded from the study.

The study population comprised of all HIV positive women, 18-69 years who had been or were sexually active and were attending the HIV clinic and consented to participate in the study. Women on their follow up for HIV who met the inclusion criteria and consented to participate in the study were screened for cervical cancer using conventional pap smear. The study instruments constituted of a questionnaire and the patients medical records. The questionnaire had structured questions which were both categorical and open ended about the socio-demographic data and sexual history while the CD4 count, HAART status and WHO stage were obtained from medical records.

Study participants from their routine HIV clinic were referred to the study room, the study was explained to them, those who were found to be eligible and were willing to participate in the study were recruited. Interviews were conducted in a safe, secure and confidential environment for those who consented to participate. The participants were recruited by consecutive sampling. The researcher/assistant was responsible for conducting all interviews, once in the interviewer room; the participant was informed about the study, its objectives, risks and benefits. Those who were willing to participate were requested to sign a written informed consent. Participants were interviewed using a questionnaire but also their medical records were checked for CD4 cell counts, if they were on HAART or not, and WHO-HIV staging double recruitment of participant was prevented by enquiring from the client if they had completed the interview before.in addition, since there was no monetary incentive given to participants, it was unlikely that a study participant would go through the process more than once.

Results

A total of 100 patients were enrolled in the study .the mean age of our participants was 34.85.youngest was 18 years and oldest was 59 years .majority of women 43 (43%) were aged between 30-39 years. Majority of our study participants had sexual debut after 16 years 88 (88%). Most participants in our study has more than 1 sexual partner 86 (86%) and those who had more than 4 lifetime sexual partners were the majority 53 (53%) as per **Table - 1**.

Table – 1: Socio-demographic characteristics.

Age in years	**No. of patients**
<20	1
20-29	23
30-39	43
40-49	26
50-59	7
Age at first sexual intercourse	
<16	12
16+	88
No. of life time sexual partners	
1	14
2-3	33
4+	53

The mean CD4 count was 805.63 with only 9 (9%) having cd4 count less than 200 cell/mm^3. Majority of our patients 74 (74%) in this study were in WHO stage I at the time of study. Most of the patients 97 (97%) were on HAART during the time of the study. A total of 100 women were enrolled in our study. The prevalence of cervical cytology abnormalities in this research was 20 (20%). LSIL being the most prevalent at 11 (11%), ASCUS 5 (5%), HSIL 2 (2%), SCC was seen in 1 (1%) and AGC-H was in 1 (1%) as per

Table - 2.

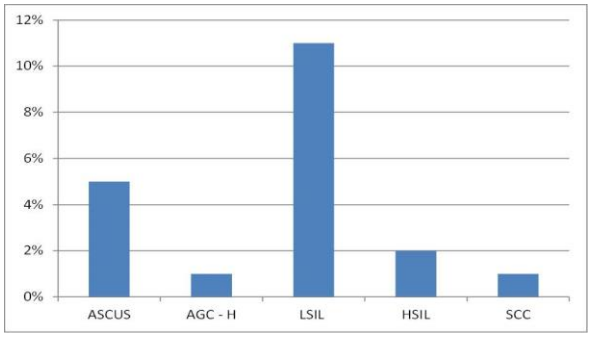
Table – 2: Clinical findings.

CD4 count	Number of patients
≤200	9
≥200	91
On ART/not	
Yes	97
No	3
WHO Stage	
I	74
II	10
III	13
IV	3

BETHESDA Classification, N=20; CD4 cell count and abnormal Pap smear, N=100, P value=0.0000697.

LSIL was the most common lesion seen among the abnormal pap smears (**Figure – 1**).

Figure – 1: Cervical cytology abnormality.



Women whose cd4 cell count was less than 200 cells/mm^3 were more likely to have abnormal pap smear P value is 0.0000697, N=100. The association between WHO STAGE and abnormal pap smear was found to be statistically highly significant p value=<0.01 as per **Table – 3**.

The association between use of HAART and abnormal pap smear was found to be statistically significant p value=0.00352.

Table – 3: Association between use of CD 4 and abnormal Pap smear.

CD4 count	Abnormal Pap smear	-ve for intra-epithelial lesion
≤200	7	2
≥200	13	78
WHO-HIV staging		
I	0	73
II	7	4
III	9	2
IV	3	0
HAART		
Yes	17	80
No	3	0

Discussion

Prevalence

The Prevalence of Cervical Cytology abnormalities were 20% (20/100). This is comparable to 18% as documented in a study done in India by Smitha N Joshi, et al. in Pune in 2003-2004 [14].

The prevalence of cervical cytology abnormalities in our study was (20%). This is comparable to 21.3% (60/280) as documented in the study done in Thailand by Pimpika Tansupswatdikul, Somkid Piyaman MD, et al. in 2009 which was aimed at establishing prevalence of abnormal cervical cytology from Pap smear in HIV-infected women [5]. The reported prevalence in this study is however higher than the 2.9% and 13.3%, reported by Kapiga, et al. [6] among HIV-seropositive pregnant women in Tanzania and Chalermchockcharoenkit, et al. [13] in Thailand among HIV-infected women by postpartum Papanicolaou smear. The fact that the other studies were conducted among pregnant and postpartum women may have contributed to the observed variation. The current study's prevalence is high compared to other researches done in Brazil (12.1%) by Patricia Abrue, et al. (2006) [7]. All studies sought to establish the prevalence, and factors associated with cervical cytology abnormalities in HIV infected women

in which the prevalence of abnormal cytology was lower compared to our findings of 20%. However, other researchers have reported higher prevalence in Africa involving HIV-positive women; In Makurdi, Nigeria (57.7%), Tanzanian 28% and South African 31% and Kenya (46%). The difference between this current study and those of other researchers may be attributed to the different social backgrounds and sample size differences and possibly the different stages of HIV infection and specific age groups sampled like in the Kenyan cohort where only patients aged 30 to 39 were recruited. Elsewhere L. Stewart Massad, et al. in their study, "Prevalence and predictors of sqaumous cell abnormalities in Papanicolaou smear from women infected with HIV" which was a multicentre prospective cohort study that was conducted in six U.S cities [15]. Cervical cytology was abnormal in 38.3% of HIV-infected women VS 16.2% of HIV-uninfected women. In one study, the prevalence of cervical abnormalities was reported to be 44% in the USA. These two were high 38.3% and 44% compared to our findings 20%, this is probably due to the large numbers used in their studies (**Table – 4**).

Table - 4: Comparison of our study with other studies.

Observations	Smitha N Joshi, et al. [14]	Jaya Chakravarthy, et al. [12]	Present study
Number of patients	287	287	100
Prevalence	18%	26%	20%
LSIL	10	32	11
ASCUS	6	3	5
HSIL	--	10	2
Squamous cells-H	2	-	--
SCC	--	3	1

CD4 count

Immunosuppression by HIV infection is a strong risk factor for abnormal cytology (SIL). In one study found that 60.9% of their 369 HIV-positive women had initial CD4 counts less than 200 cells/mm^3. The lower percentage of women with immunologic AIDS in this study may partly explain the lower prevalence of SIL of 20% in this study as compared with 29% in the Jos study. This study also showed that the CD4 count was inversely associated with cervical cytology abnormalities, and women with a CD4 count less than 200 cells/mm3 were at greater risk of abnormal cytology compared to women with CD4 counts greater than 200 cells/mm^3. This finding is in accordance with several other studies involving HIV-positive women. Prolonged CD4 lymphopenia in patients infected with HIV results in defective T-cell proliferation regardless of the current CD4 count or viral load. Davis et al. reported that the strongest predictor of genital dysplasia was a nadir CD4 and CD4 count less than 200 cells/mm^3 [8].

Use of HAART

In a study done in 5 cities in USA by Minkoff, et al. [9] published in 2001 women on HAART were 40%. More likely to demonstrate regression and less likely to demonstrate progression. The Canadian women's HIV study done in 2002 published in journal of infection diseases in 2013 a total of 467 of 456 women were included in the longitudinal cervical cytopathlogic and HPV DNA analyses respectively HIV positive women held used prevalence (46.6% Vs 28.7) used aquisition and used clearance of oncogenic HPV compared to HIV negative. Oncogenic HPV predicted prognosis of cervical dysplasia from normal to abnormal SIL. HAART increased the regression of cervical SIL and increased clearance of oncogenic HPV types other that 16 or 18. This analyst demonstrated beneficial effects of HAART on cervical SIL in HIV

positive cases. Previous studies have not satisfactorily established a protective effect of antiretroviral treatment on the risk of SIL. HAART showed some potential effect in the women's interagency HIV study [9]. Heard, et al. [10] showed that HAART had a positive impact on regression of SIL, and this was associated with increasing CD4 cell counts. In one study found that patients who were not on ART were 2.21 times more likely to have CIN infection than patients who were not on HAART. In other studies, the effect of HAART on the prevalence of SIL has not been significant or it has remained unchanged. Similarly in this study, the use of HAART was not associated with a significant reduction in the risk of SIL In other studies the effect of HAART on the prevalence of SIL has not been significant or the prevalence of SIL has remained unchanged. In one study risk factors such as drug use, parity, age at first intercourse, number of partners, educational status were not associated with abnormal cervical cytology. Many studies have been reported regarding the prevalence of pap smear abnormalities in HIV seropositive women. In a cross sectional study done in Zambia published in 2015 among 309 HIV positive women to measure cervical disease burden by visual inspection with acetic acid enhanced by Digital Cevicography, cytology and histology over half (52%) were screened positive by DC, while 45% had cytologic evidence of HSIL or worse. HPE revealed 20% of women had evidence of CIN2 or worse, 11% had CIN3 or worse, 2% had ICC [11].

In a study done in India by Jaya Chakravarthy, et al. published in 2016, 216 HIV positive women were screened 58 (26.85%) were HPV-Positive, 56 (25.9%) were of high risk HPV type. The most prevalent HPV type was HPV-16 (7.9%) non 16 and 18 HPV types were present in 17.6% patients. 139 (74.33%) patients had normal/ negative for intraepithelial lesions, three (1.60%) had ASCUS, 32 (17.11%) had LSIL, 10 (5.35%) had HSIL and (1.60%) had ca. cervix .WHO clinical stage III and IV and CD4 <_350/ul were risk factors for abnormal cytology [12]. In a study done in Thailand by Chalermchocharoenkit, et al. (2010) to establish the prevalence, and factors associated with cervical cytology abnormalities in 821 HIV infected Thai women at a female sexually transmitted disease clinic, Faculty of Medicine Siriraj Hospital, Mahidol University, the prevalence of sqaumous cell abnormalities was 15.4% (SCA); ASCUS:2.8%, ASC-H:0.6%, LSIL:8.5%, HSIL:3.5% [13]. In another study done in Thailand in 2008 published in 2009, the prevalence of abnormal cervical cytology from Pap smear in 280 HIV-infected women was 21.3% (60/280) of which 0.7% (2/280) had atypical squamous cells exclude high grade lesion (ASC-H), 6.4% (18/280) had low grade squamous intraepithelial lesion (LSIL), 12.1% (34/280) had high – grade squamous cell intraepithelial lesion (HSIL) and 2.1% (6/280) had squamous cell carcinoma (SCCA) [5].

Conclusion

In conclusion, a high prevalence (20%) of cervical cytology abnormality was found among HIV infected women. Decreased CD4 cell counts were associated with abnormal Pap smear. CD4 cell counts less than 200 cells/mm3 was significantly associated with positivity of the cervical cytology. There was no statistically significant association between WHO stage and abnormal Pap smear.

References

1. GLOBOCAN 2012, Cancer Incidence and Mortality Worldwide in 2012: IARC.
2. Munoz N, Bosch F, de Sanjose S. Epidemiologic classification of human papillomavirus types associated with cervical cancer. New England Journal of Medicine, 2003; 348: 518–527.
3. Clifford G, Smith J, Plummer M, Munoz N, Franceschi S. Human papillomavirus types in invasive cervical cancer worldwide: a meta-analysis. British Journal of Cancer, 2003; 88: 63–73.
4. Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a

necessary cause of invasive cervical cancer worldwide. J Pathol., 1999; 189(1): 12-9. .

5. Pimpika Tansupswatdikul, Somkid Piyaman, et al. Prevalence and Predictors of Abnormal Cervical Cytology in HIV-Infected Patients at the Anonymous Clinic, Chonburi Hospital. Thai Journal of Obstetrics and Gynaecology, 2009; 17: 51-5661.
6. Kapiga SH, Msamanga GI, Spiegelman D, Mwakyoma H, Fawzi WW, Hunter DJ. Risk factors for cervical squamous intraepithelial lesions among HIV-1 seropositive women in Dar es Salaam, Tanzania. Int J Gynecol Obstet., 1999; 67: 87–94.
7. Patrıcia Abreu Pinheiro de Lemos, Marco T´ulio Antonio Garcıa-Zapata, et al. Cervical Cytopathology in a Population of HIV-Positive and HIV-Negative Women. Journal of Tropical Medicine, 2012, Article ID 869758, 4 pages doi:10.1155/2012/869758.
8. Davis AT, Chakraborty H, Flowers L, Mosunjac MB. Cervical dysplasia in women infected with HIV: a correlation with HIV viral load and CD4 count. Gynaecol Oncol., 2001; 80: 350–354.
9. Minkoff H, Ahdieh L, Massad LS, et al. The effect of highly active antiretroviral therapy on cervical cytologic changes associated with oncogenic HPV among HIV-infected women. AIDS, 2001; 15: 2157–2164.
10. Heard I, Tassie JM, Kazatchkine M, Orth G. Highly active antiretroviral therapy enhances regression of cervical intraepithelial neoplasia in HIV-seropositive women. AIDS, 2002; 16: 1799–1802.
11. Bateman, et al. Burden of cervical precancer and cancer in HIV Positive women in Zambia 15: 54, DOI 10.1186/s12885-015-1558-5.
12. Jaya Chakravarthy, et al. Prevalence of HPV infection and cervical abnormalities in HIV positive women in Eastern india, IJMR, 2016; 143(1): PMC4822373.
13. Chalermchockcharoenkit A, Chenchit Chayachinda, et al. Prevalence and cumulative incidence of abnormal cervical cytology among HIV-infected Thai women. BMC Infectious Diseases, 2011; 11: 8.
14. Joshi SN, et al. Cost-effectiveness of a repeat HIV test in pregnancy in India. BMJ open, 2015; 5(6): e006718.
15. Massad LS, Riester KA, Anastos KM, et al. Prevalence predictors of squamous cell abnormalities in Papanicolaou smears from women infected with HIV-1. Women's Interagency Study Group. J Acquir Immune Defic Syndr, 1999; 21: 33-41.