Prevalence of Cervical Dysplasia among Women attending an HIV Care Center in Chennai, South India

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OBJECTIVE - To find out the prevalence of cervical squamous intraepithelial lesion (SIL), the precursor of cervical cancer, among HIV – seropositive and high-risk HIV – seronegative women attending an HIV care facility in Chennai. **METHODS -** One hundred and forty women (93 HIV +ve and 47-ve) were studied. The demographic data was collected along with history of lower genital tract infections (LGTI) and obstetric and menstrual history. Each woman had a pelvic examination and specimens collected for screening for LGTI and had Pap smears taken. Statistical analysis was used to determine the correlation between prevalence of abnormal Pap smears and demographic and clinical variables, including CD4 counts. **RESULTS -** Twenty-four (17.1%) Pap smears were abnormal; 12 (8.6%) had atypical squamous cells of undetermined significance (ASCUS), 8 (5.7%) were low grade SIL (LGSIL) and 4 (2.9%) were high grade SIL (HGSIL). The finding of SIL was not significantly associated with HIV infection or CD4 counts. SIL was significantly associated with the presence of lower genital tract infections (LGTIs), particularly Chlamydia infection. **CONCLUSION -** Our findings suggest a need for screening of LGTI and cervical abnormalities for cervical dysplasia.

Key words : cervical dysplasia, Pap smears, HIV, lower genital tract infections, prevalence of cervical dysplasia

Introduction

Human immunodeficiency virus (HIV) infections are now increasing rapidly in women in the developing world, comprising 40% of all new infections[1]. Seventy-five percent of all cases of cervical dysplasia occur in developing countries[2]. Risk factors for cervical dysplasia include sexual intercourse at an early age, multiple sexual partners and partners with multiple sexual partners[3]. Cervical cancer is known to be more common and aggressive in iatrogenically immunodeficient women[4]. A meta-analysis of five case-controlled studies in developing countries found that the overall odds ratio between HIV infection and developing cervical dysplasia was 4.9[5]. In Chennai, cervical cancer is the leading cancer among all women and the second most common cancer among women of ages 15 – 34 years[6]. The main purpose of this study was to assess the prevalence of cervical SIL among HIV seropositive and high-risk HIV seronegative women.

Material and Methods

One hundred and forty women (93 HIV infected and 47 HIV seronegative) were enroled in the study to screen for cervical dysplasia from April 1999 through May 2000 at YRG CARE center in Chennai. HIV seropositive women enrolled were either partner of the male patients receiving treatment at the center or were referrals to our center. HIV uninfected women were partners of HIV infected men. Women who had previously undergone total hysterectomy were excluded from the study.

At enrolement, all participants gave informed consent and were interviewed with a structured questionnaire on their demographic profiles and gynecologic and obstetric history including sexually transmitted diseases (STDs). They underwent pelvic examinations with Pap smear and screening for selected lower genital tract infections (LGTIs). Pap smears were analyzed according to the Bethesda classification system. Smears were read by a single cytopathologist without knowledge of the subject's clinical or serologic status. The study protocol was reviewed and approved by YRG CARE Center and Brown University (Providence, RI USA) institutional review boards.

Statistical Methods

Data management was done in Microsoft Access. All statistical analysis was conducted in SPSS 9.0. To compare the demographic and clinical variables, including any LGTIs, with cervical smear results, the chi-square test was used. Descriptive statistics were run for cervical smear results and HIV status. Statistical significance was determined by p< 0.05, odds-ratios (OR) and 95% confidence interval (CI).

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Results

The age range of the women was 15-42 years (mean=27 years), and 50.6% of them were over 25 years. In this cohort, 93 women (66.4%) tested HIV seropositive and 47 (36.3%) seronegative. The mean age of first coitus was 19 years. The median CD4 counts among 93 HIV infected women was 627 cells / mm^3 (Range : 6-2670). Chlamydia was the most common LGTI (Table I).

Clinical and Cytological Findings

One hundred and sixteen (82.8%) of the 140 women had Pap smears within normal limits (WNL) (Table II). Among the abnormal results, there were 12 (8.6%) ASCUS (atypical squamous cells of undetermined significance), 8 (5.7%) LGSIL (low-grade squamous intraepithelial lesion) and 4 (2.9%) HGSIL (high-grade squamous intraepithelial lesion). Twelve women (8.6%) had visible, external genital warts, of whom seven were HIV seropositive. We found no significant associations between the presence or severity of SIL and HIV infection or CD4 counts.

Table I : LGTIs Among Women with SIL

Infection	SIL +	SIL -	p-value
Chlamydia (N=46)	8 (66.7)	38 (29.7)	0.012
Vaginal Candida (N=32)	5 (41.6)	27 (21.1)	0.105
Cervical Ulcers (N=29)	4(33.3)	25(19.5)	0.259
Bacterial Vaginosis (N=23)	3(25.0)	20(15.6)	0.402
Genital Ulcers (N=13)	1(8.3)	12(9.3)	0.905
Genital Warts (N=112)	0 (0.0)	12 (8.6)	0.663
HSV (N=7)	2 (16.6)	5 (3.9)	0.07
Syphilis (N=5)	0 (0.0)	5 (3.9)	0.372
Gonorrhea (N=4)	0(0.0)	4(3.1)	0. 534
Trichomonas (N=3)	0(0.0)	3(2.3)	0.445

Table II : Pap Smear Results by HIV Status

Pap Smear Reading[a]	HIV + (N=93)	%	HIV - (N=47)	%	p-value Overall : 0.86
WNL	77	82.8	39	82.9	0.98
ASCUS	7	7.5	5	10.6	0.54
LSIL	6	6.5	2	4.3	0.72
HSIL	3	3.2	1	2.1	0.99

[a] Bethesda classification

Table III : Cervical Inflammation and Pap Smear Results

Pap smear reading[a]	Inflammation N=57 (%)	No Inflamation N=83(%)
WNL	38 (66.7)	78 (94.0)
ASCUS	12 (21.0)	0
LSIL	5 (8.8)	3 (3.6)
HSIL	2 (3.5)	2 (2.4)

[a] Bethesda classification

There was significant association between SIL smears and current LGTIs (p= 0.042, OR = 2.88, CI = 0.95 – 10.48) (Table I). Eighty five (60.7%) of the 140 women tested positive for an LGTI. Eleven (91.7%) of the 12 women with dysplasia (low and high grade) had an LGTI. Women with cervical SIL had an eight fold increased risk of LGTIs compared to women without SIL (p=0.022, OR = 8.03, CI 1.006 14.05). Chlamydia was significantly associated with abnormal smears (p= 0.001, OR = 4.35, CI = 1.59-12.17). Two (50%) of the four women with HGSIL were HIV seropositive. Of the eight seronegative women with abnormal smears, seven (87.5%) had an LGTI (p= 0.044, OR = 7.37, CI=0.76-174.9), particularly Chlamydia infection (p=0.00019, OR = 29.0, CI = 2.68-742.7).

One important finding was a high 40.7% (57/140) of Pap smears showed inflammation. (Table III). There was a significant association between inflammation and abnormal smears (p< 0.001). Nineteen of the 24 (79.2%) women with abnormal smears had inflammation.

Discussion

It has been shown previously that women infected with HIV have a higher rate of cervical SIL than seronegative women of similar backgrounds[7]. Studies have shown significant association between risk for cervical SIL and HIV infection in women attending family planning clinics in Kenya[7] and Malawi[8]. A prospective study of SIL in 239 women in Delhi reported a 23% progression from mild lower-grade SIL to malignancy after 132 months[9].

We did not find significant association between cervical SIL and HIV infection. There are several possible explanations for this. First, our sample population is different from previous studies that included sex workers, sexually active adolescents, or women with severe immunosuppression (CD4< 200)[10]. Eighty percent of the women in our cohort were monogamous housewives with a single lifetime sexual partner. Women other than housewives (N=28) had five times greater risk of developing SIL (p=0.007). Secondly, the small number of women with SIL (N=12, 8.6%) and the small sample size of our study prevents any decisive conclusions about prevalence of cervical SIL and HIV in the general population in India.

We did not find significant correlation between SIL status and CD4 counts as reported elsewhere[11]. Only 13% of the HIV infected women in our study had CD4 counts < 200, compared to over 60% with CD4 counts >500. An Italian study of 51 HIV positive women also found no significant association with CD4 counts[12].

Cervical SIL was correlated with the presence of LGTI, particularly Chlamydia infection. While few women in our study had low or high grade SIL, over 60% had an LGTI. A study of HPV type-16 prevalence among 50 LGT–infected and 30 healthy women at an STD clinic in India detected HPV type 16 in 30% of the women with Chlamydia infection which was significantly higher than among the 30 controls[13]. Another limitation of our study was the lack of HPV screening, which is unavailable in many developing countries. Further studies are needed to monitor disease progression to clarify the epidemiological and clinical profiles of SIL and cervical cancer and HIV infection in India.

Inflammation is a common finding on Pap smear reports but its significance is unclear. Studies have implicated microbes in inflammatory smears, particularly Chlamydia, HSV, and trichomonas vaginalis[14]. We found a significant association between inflammation and Chlamydia infection.

Though HIV management is becoming more effective and available around the world, the incidence of HIV infection in women in India is soaring while the prevalence of cervical cancer and HPV among HIV infected women is unknown. Poor health care and lack of education limit women from accessing basic medical services, including cervical screening. While routine HPV DNA screening is not feasible in the developing world, Pap smears are important, inexpensive, and accessible tools in resource-poor settings where cervical cancer related mortality is highest[1]. Providing women with Pap smears even every three years reduces the incidence of invasive cervical cancer by 90.8%[1]. Reducing the rates of cervical cancer and HIV for women in India means providing comprehensive and routine gynecologic care that emphasizes prevention, education, early detection and treatment. Our study also emphasizes the need for screening and treatment of lower genital tract infection.

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